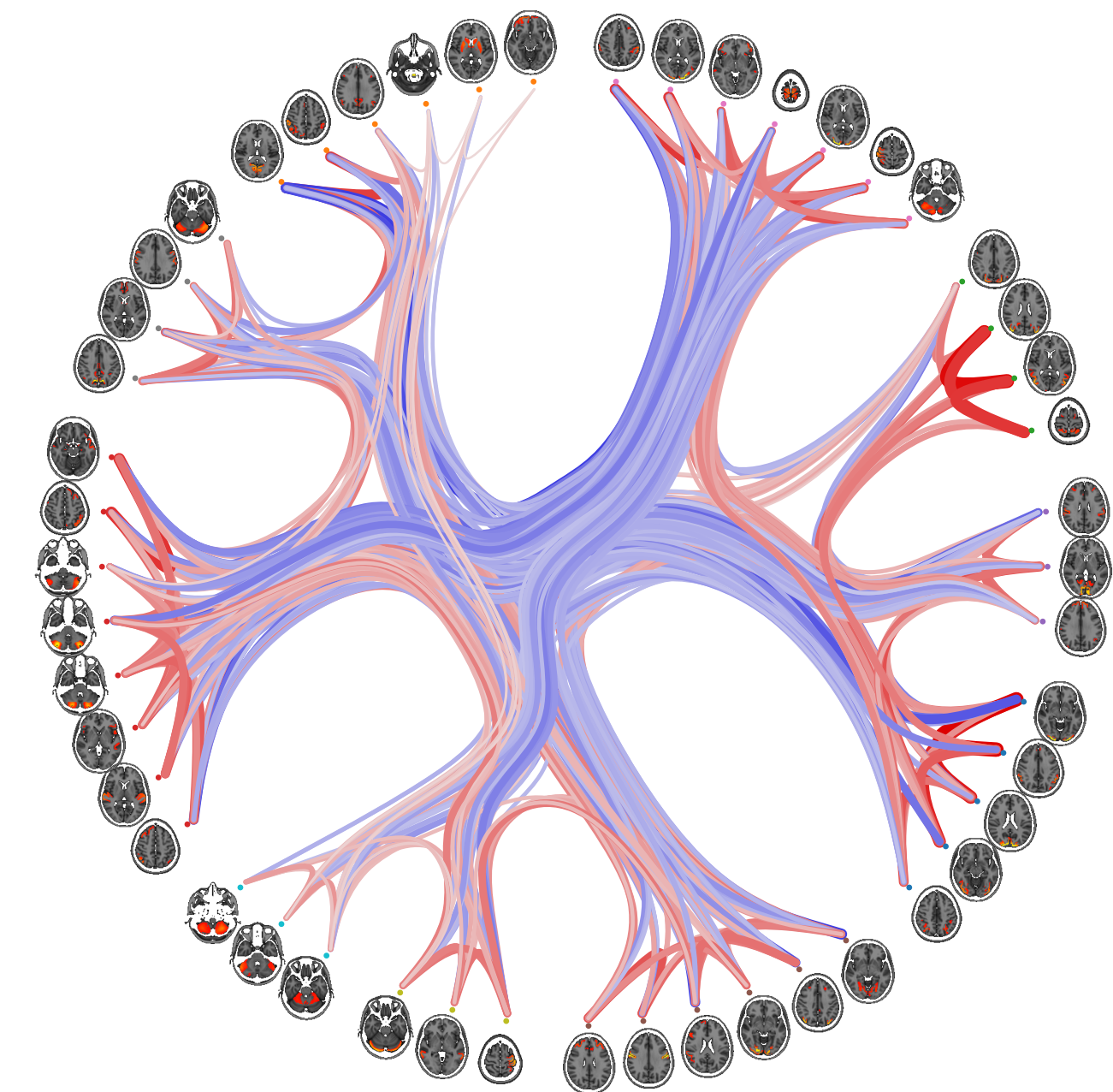
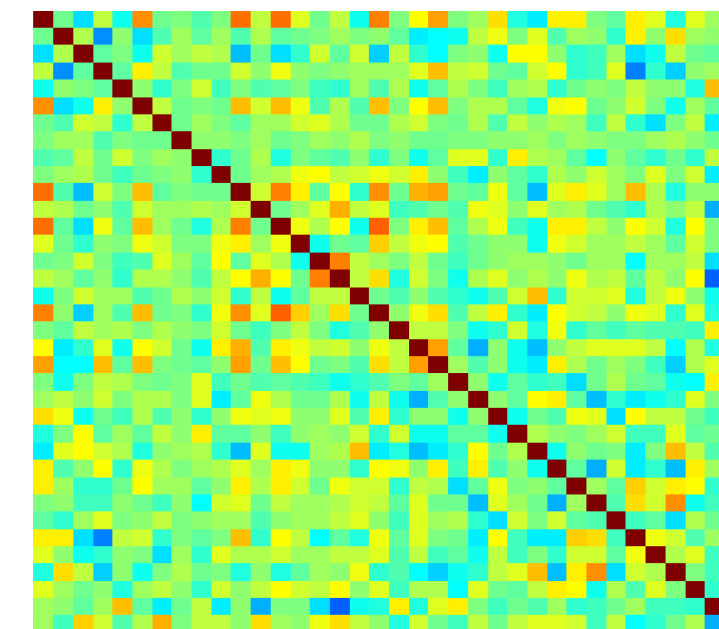


Network modelling analysis

脑网络分析

- Resting state data characteristics 静息态数据特征
- Preprocessing 预处理
- Network modelling analysis 网络建模
- Methods comparisons and considerations 方法比较和注意事项

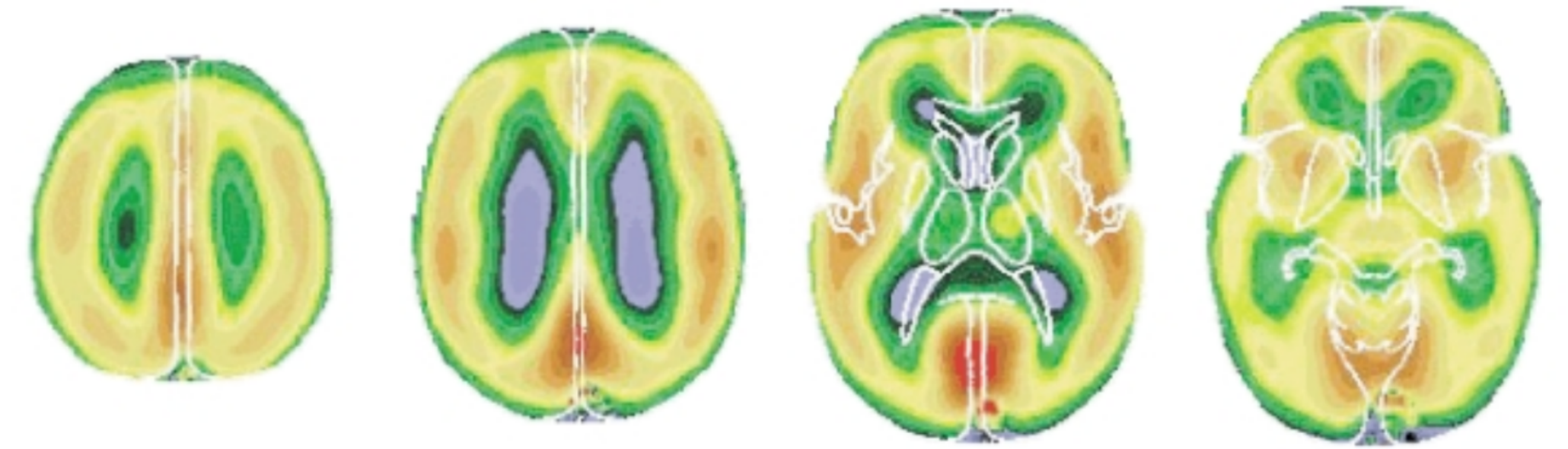


Energy consumption in the brain

大脑的能量消耗

- Brain < 2% body weight but consumes ~20% of total energy
大脑重量约占身体的<2%,但却消耗约20%的总能量
- estimated 60-80% of this energy used to support communication between cells
约60-80%的能量用于细胞间的交流
- task-evoked activity accounts for ~1%
任务诱发的脑活动约占1%

Oxygen consumption 耗氧量

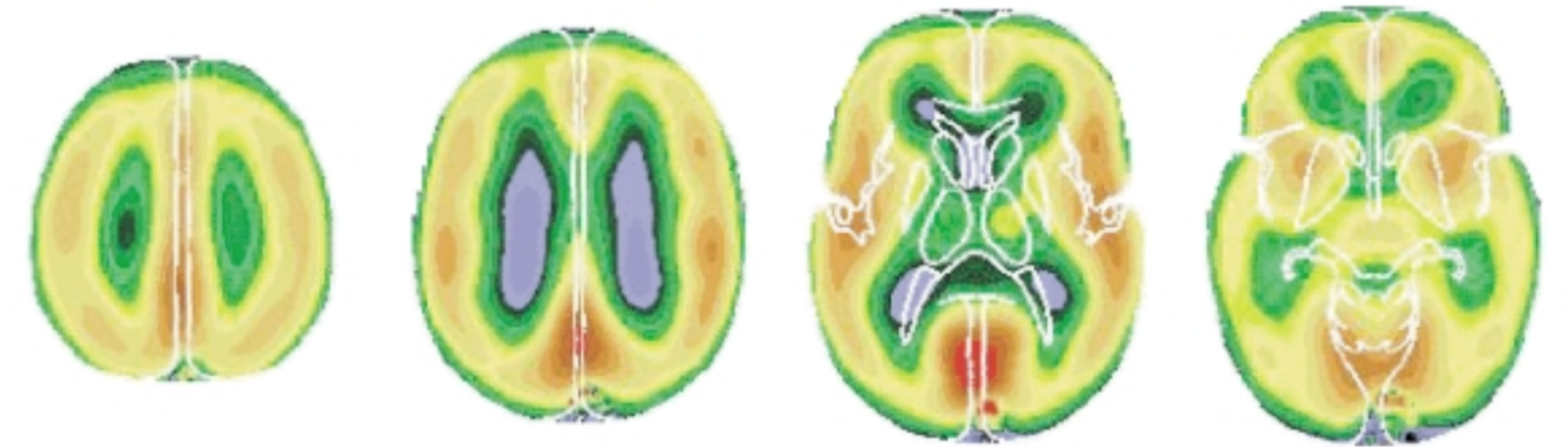


Energy consumption in the brain

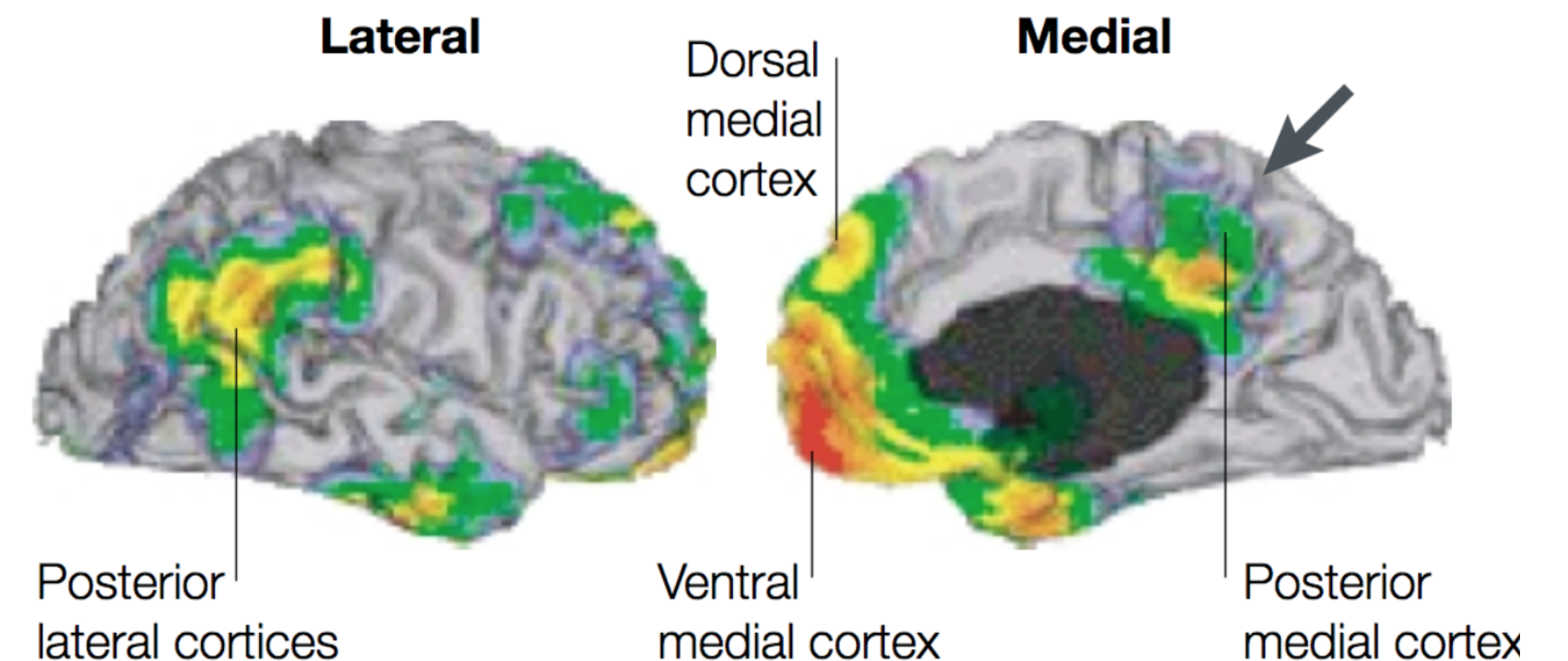
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Oxygen consumption 耗氧量



Decreased activity during tasks (PET)
执行任务时脑活动下降

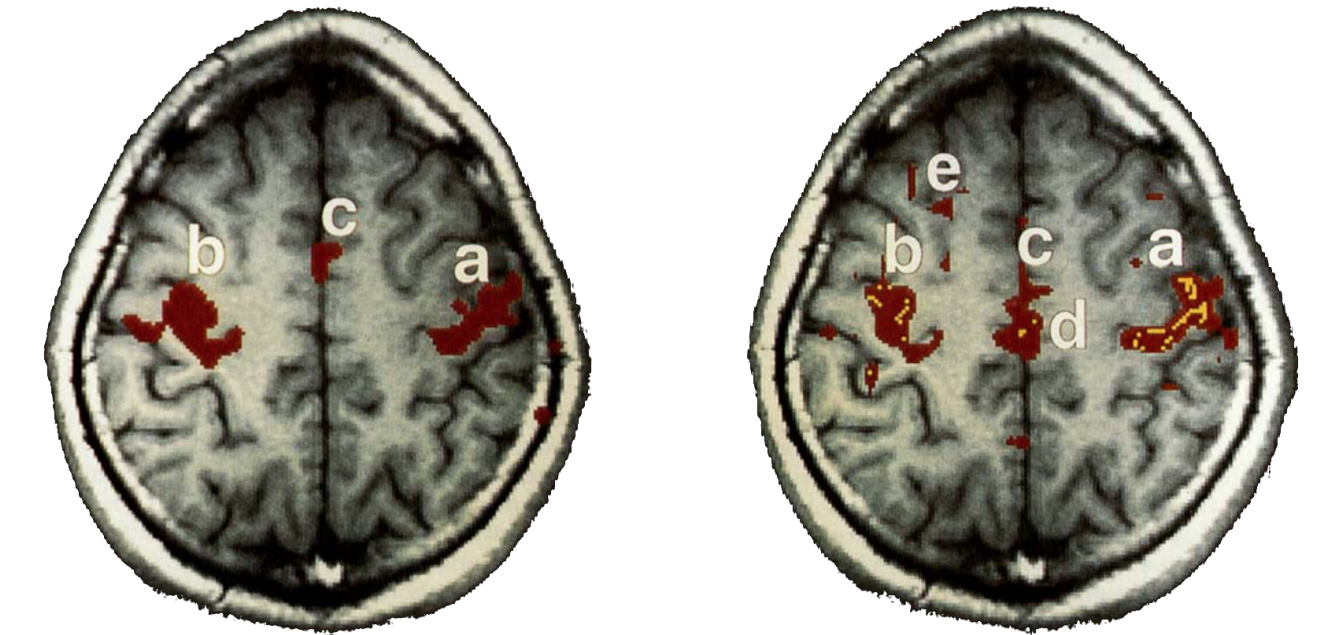


Why study the brain at rest?

为什么研究大脑的静息态

- Localisation versus connectivity 定位与连接
- Understand the inherent functional organisation of the brain 了解大脑固有的功能活动

Finger tapping 手指活动 Rest 静息态

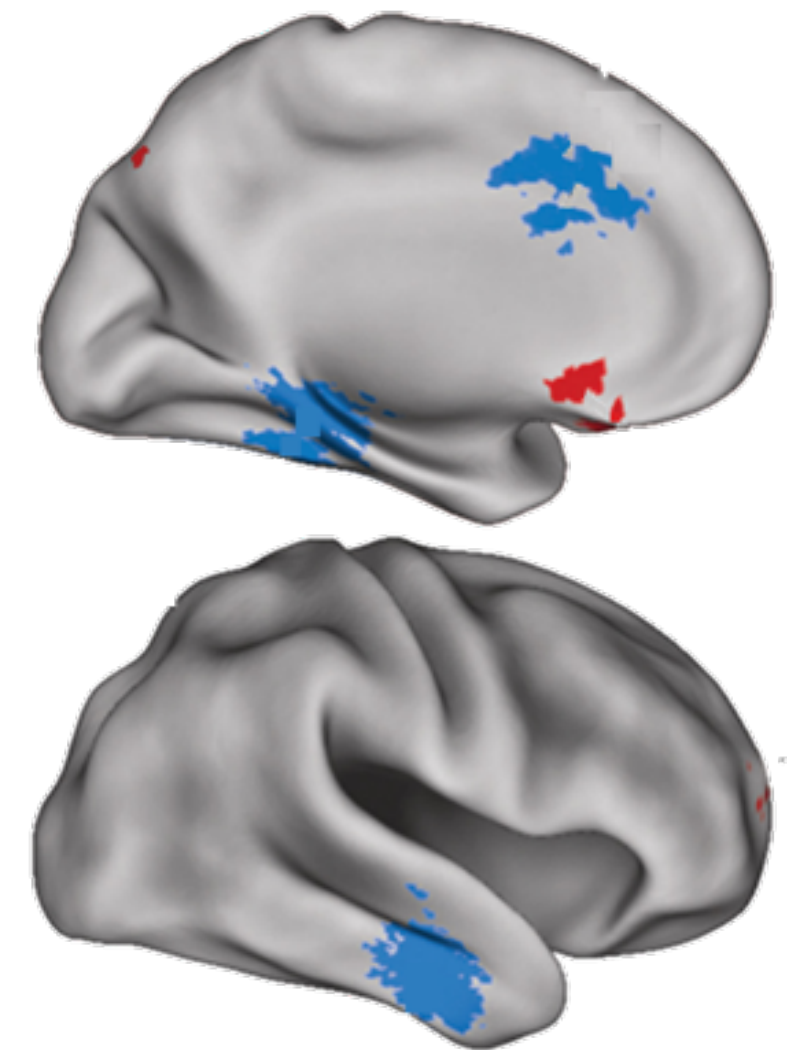
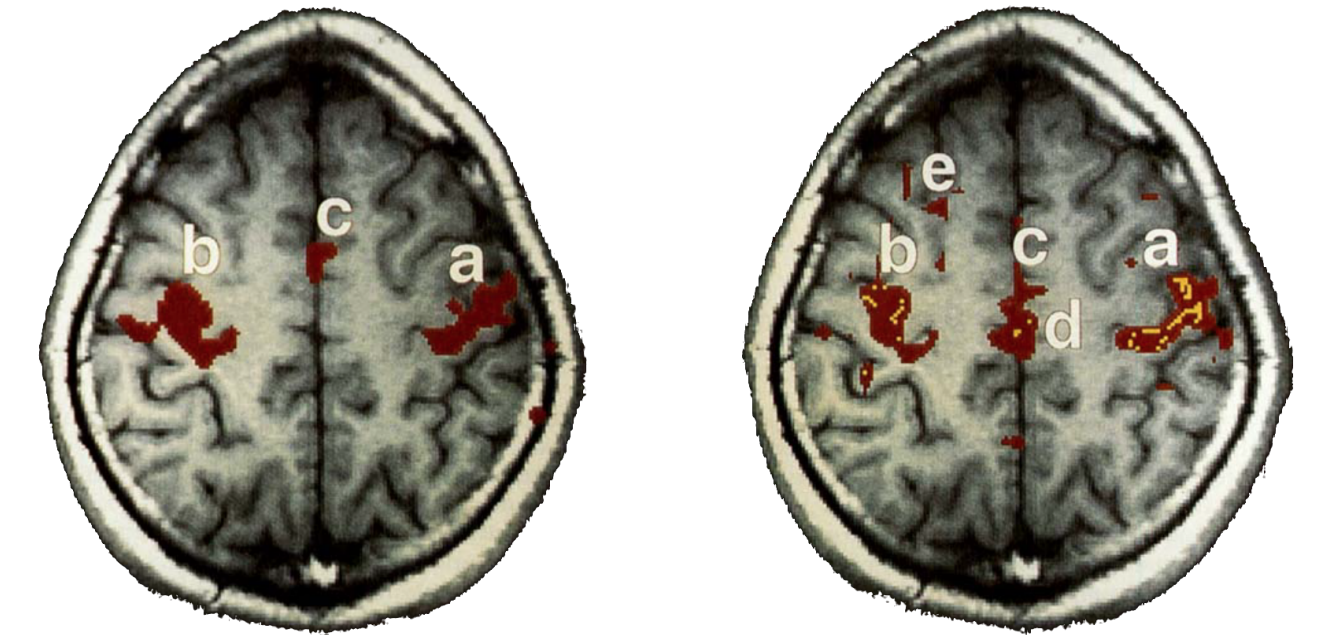


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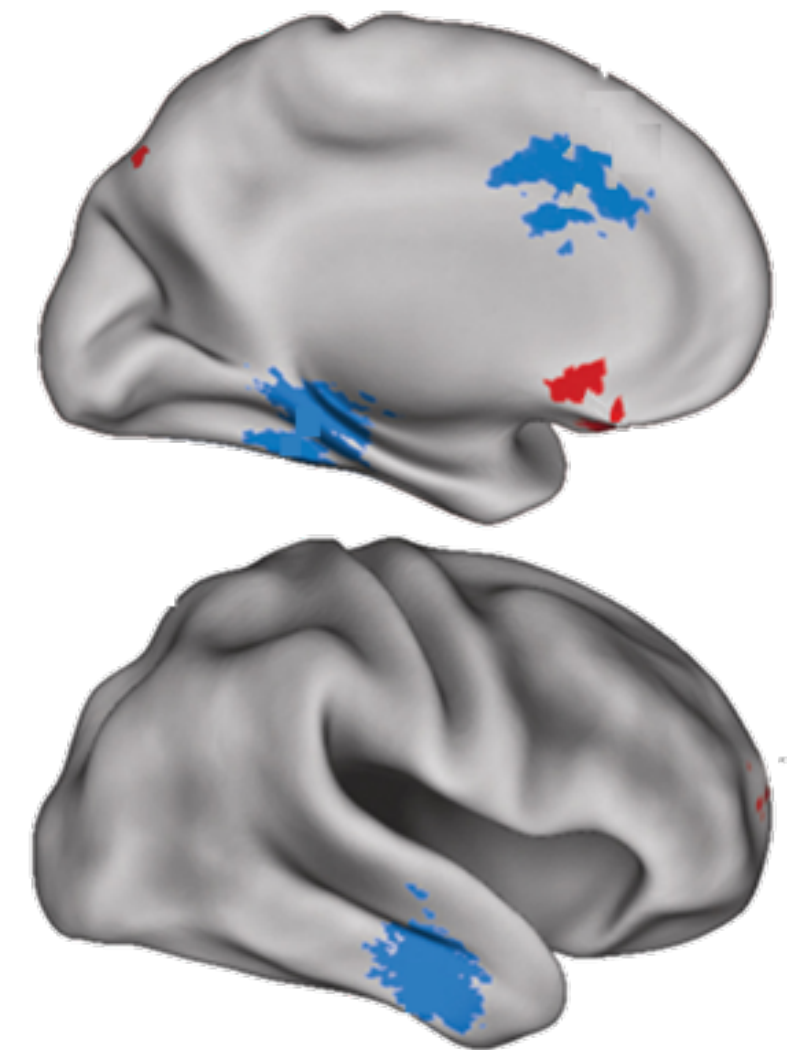
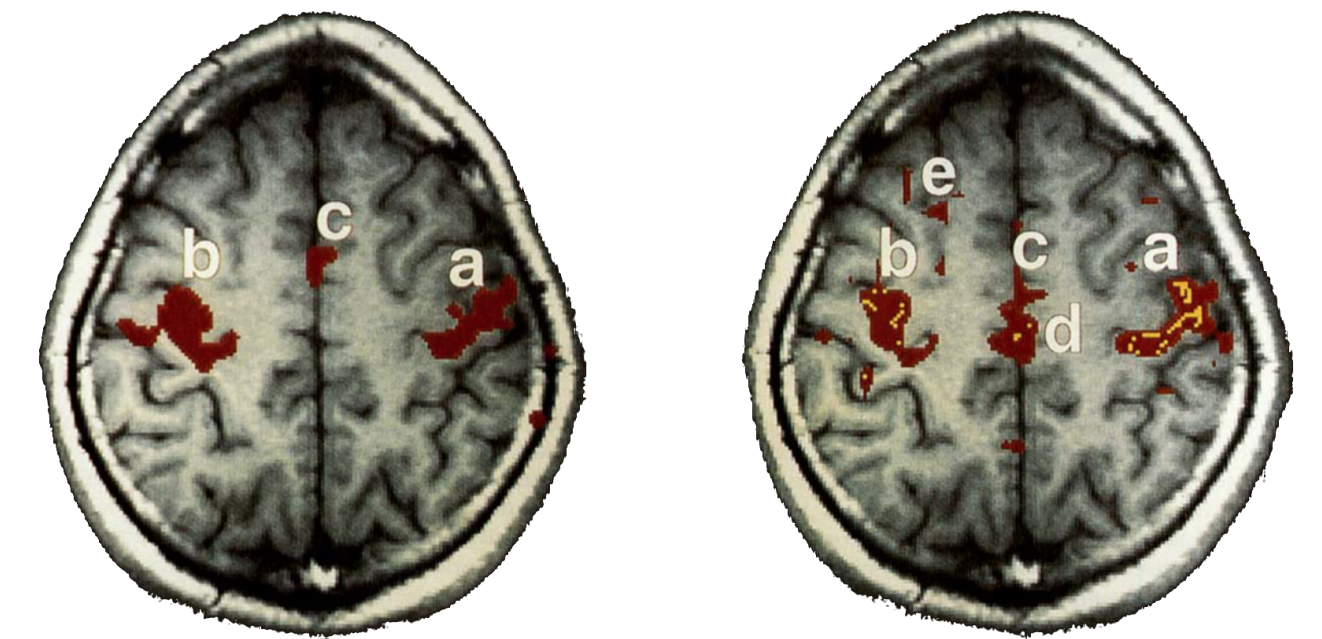


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- Understand the inherent functional organisation of the brain 了解大脑固有的功能活动
- Clinical/ cognitive biomarker 临床/认知标记
- Pragmatic benefits: can be done in any population, with relatively little setup and expertise required 实用的优点：可以在任何人群中完成，只需要相对较少的设置和专业知识

Finger tapping 手指活动 Rest 静息态





Resting state data analysis

静息态数据分析

- Many different methods available for analysis
可用许多不同的分析方法
- All have one assumption in common: 它们共同的假设:
- i.e. Definition of functional connectivity is based on a statistical dependency between time series
功能连接的定义是基于时间序列之间的统计依赖性
- Differences between methods lie in the way these similarities are estimated and/or represented
方法之间的差异在于估计和/或表示这些相似性的方式

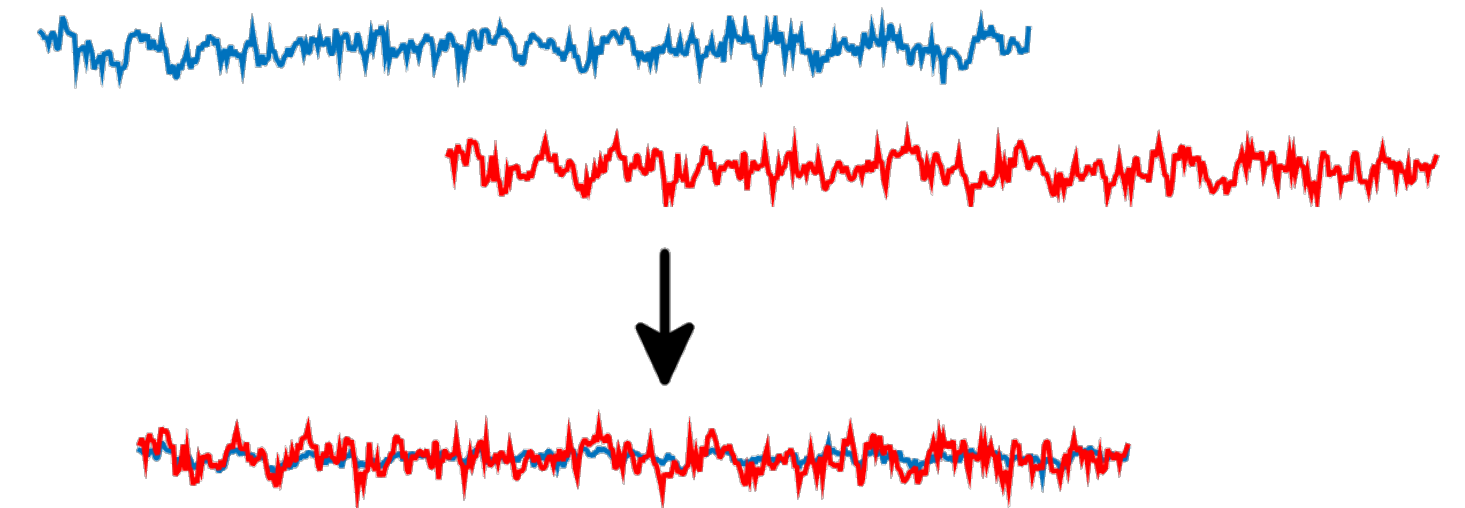
If two brain regions show similarities in their BOLD timeseries, they are functionally connected

如果两个大脑区域在其BOLD时间序列中显示出相似性，则它们在功能上是相互关联的

Types of connectivity

连接的类型

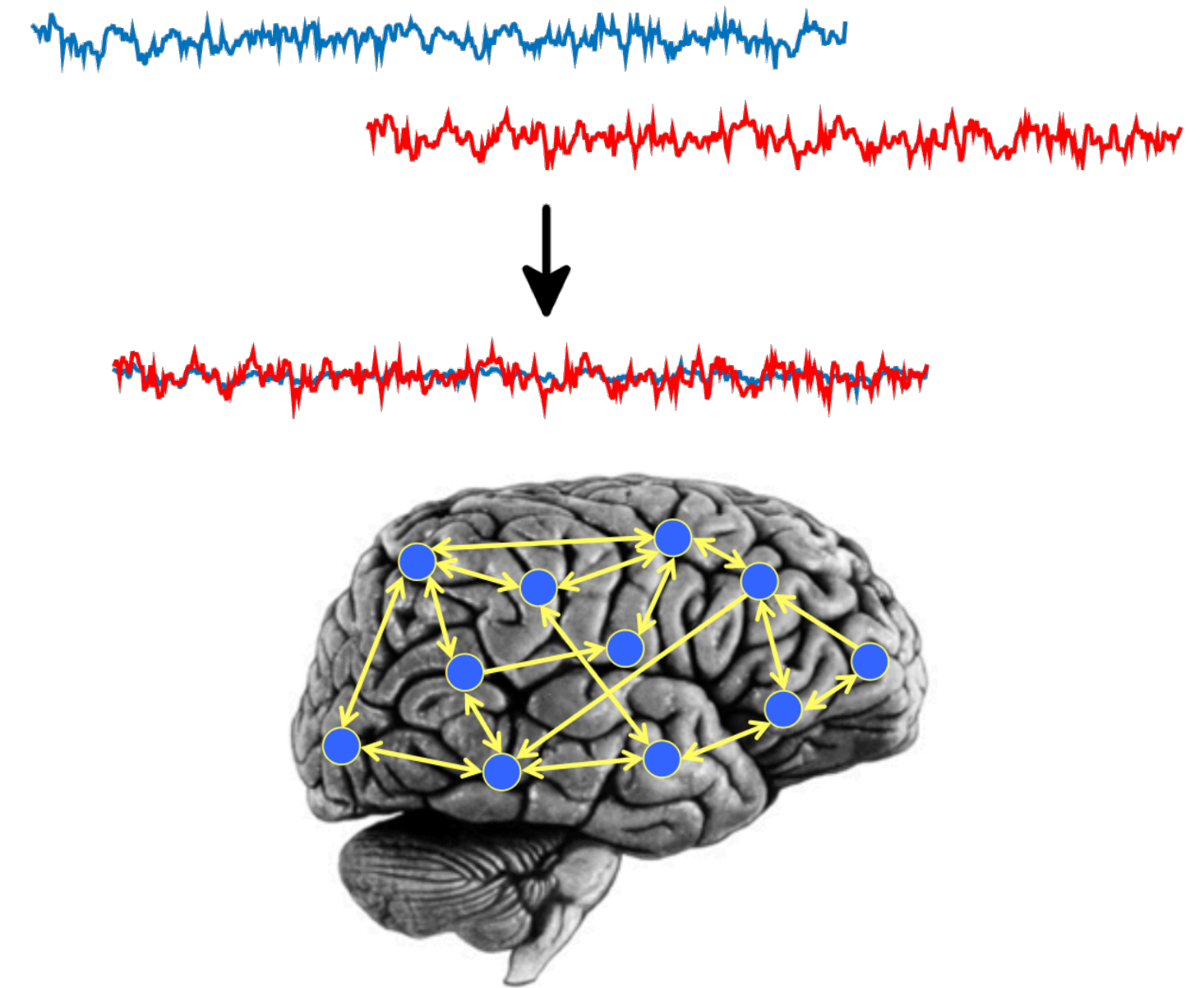
- Functional connectivity 功能连接
- Statistical dependency 统计依赖性
- Effective connectivity 有效连接
- Directional influence 方向的影响
- Anatomical (structural) connectivity 结构连接
- Presence of a white matter tract 白质纤维束



Types of connectivity

连接的类型

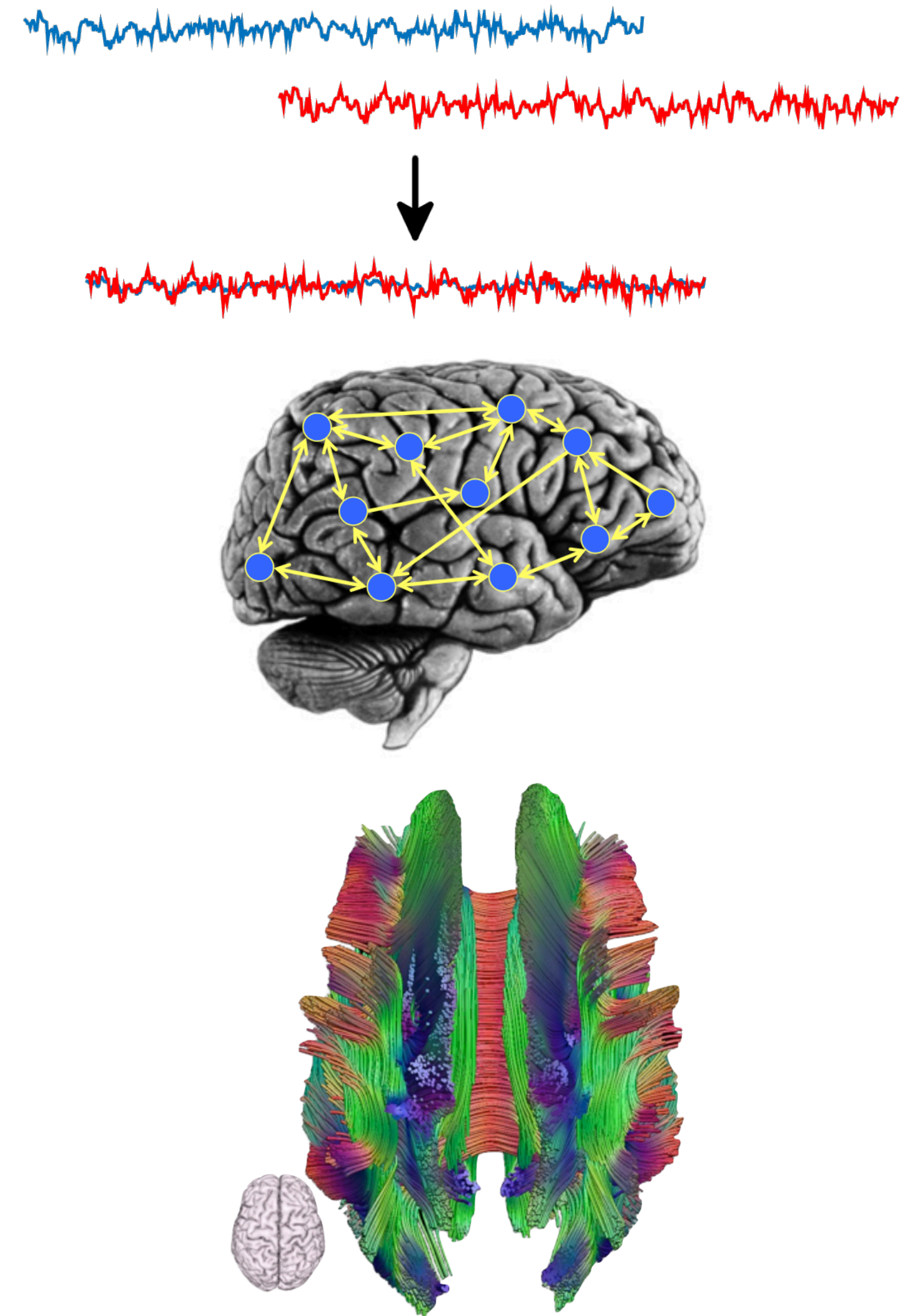
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Data characteristics

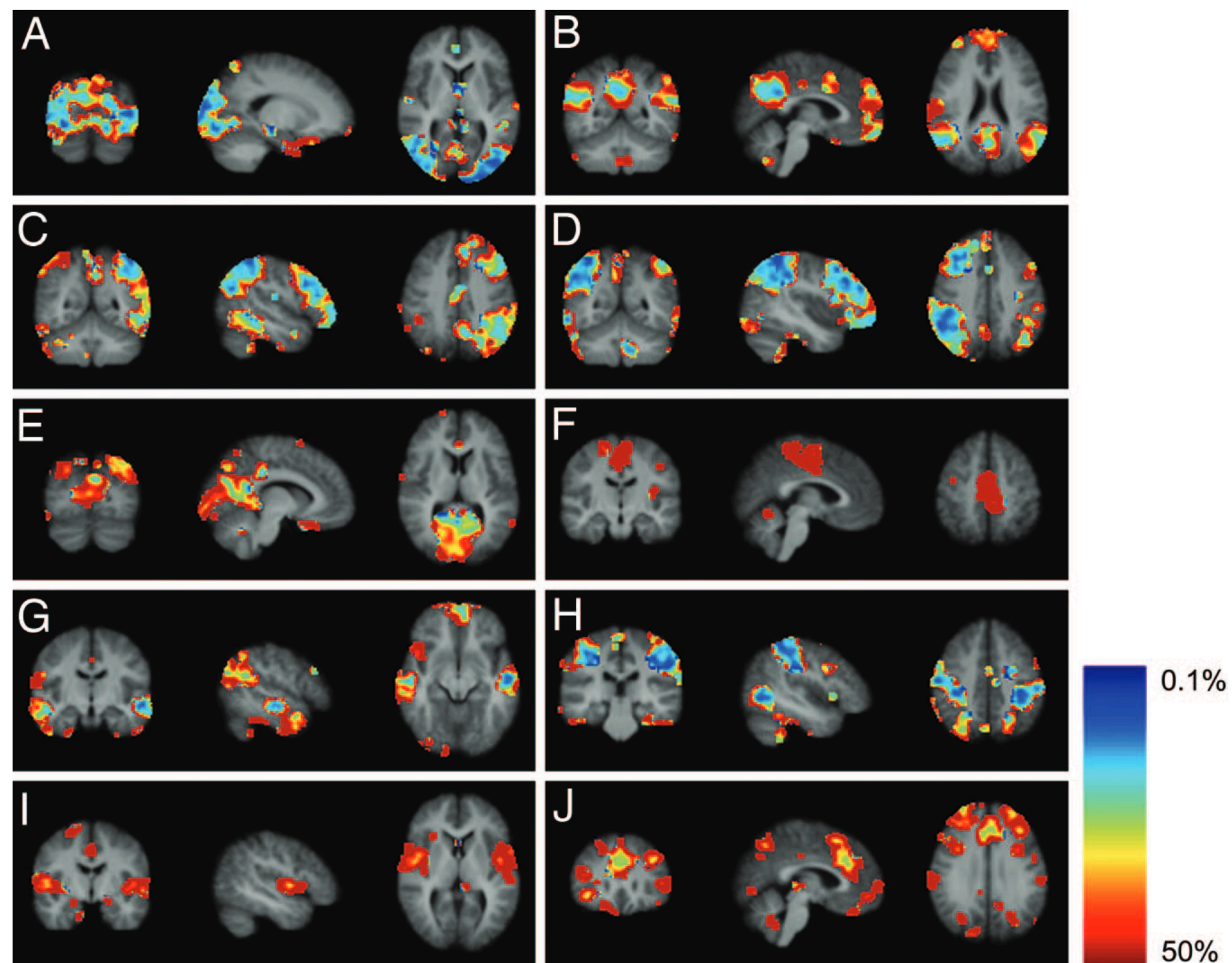
数据特征

Replicable networks

可重复的网络

Large-scale inherent organisation is reproducibly found across studies and approaches

多种研究和方法可重复地发现脑内存在大规模的固有组织

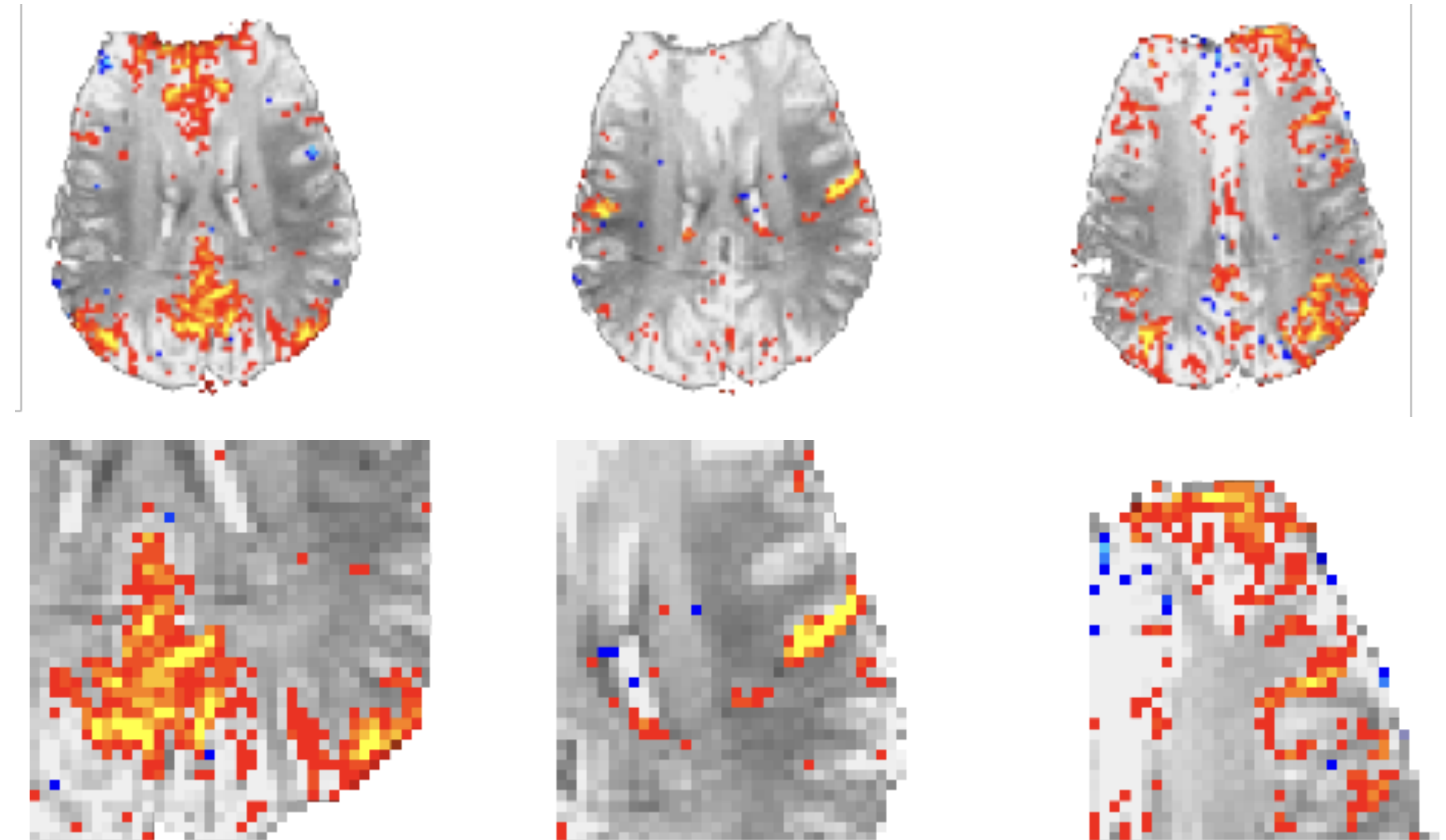


Grey matter networks

灰质网络

Resting state network structure
is localised in grey matter

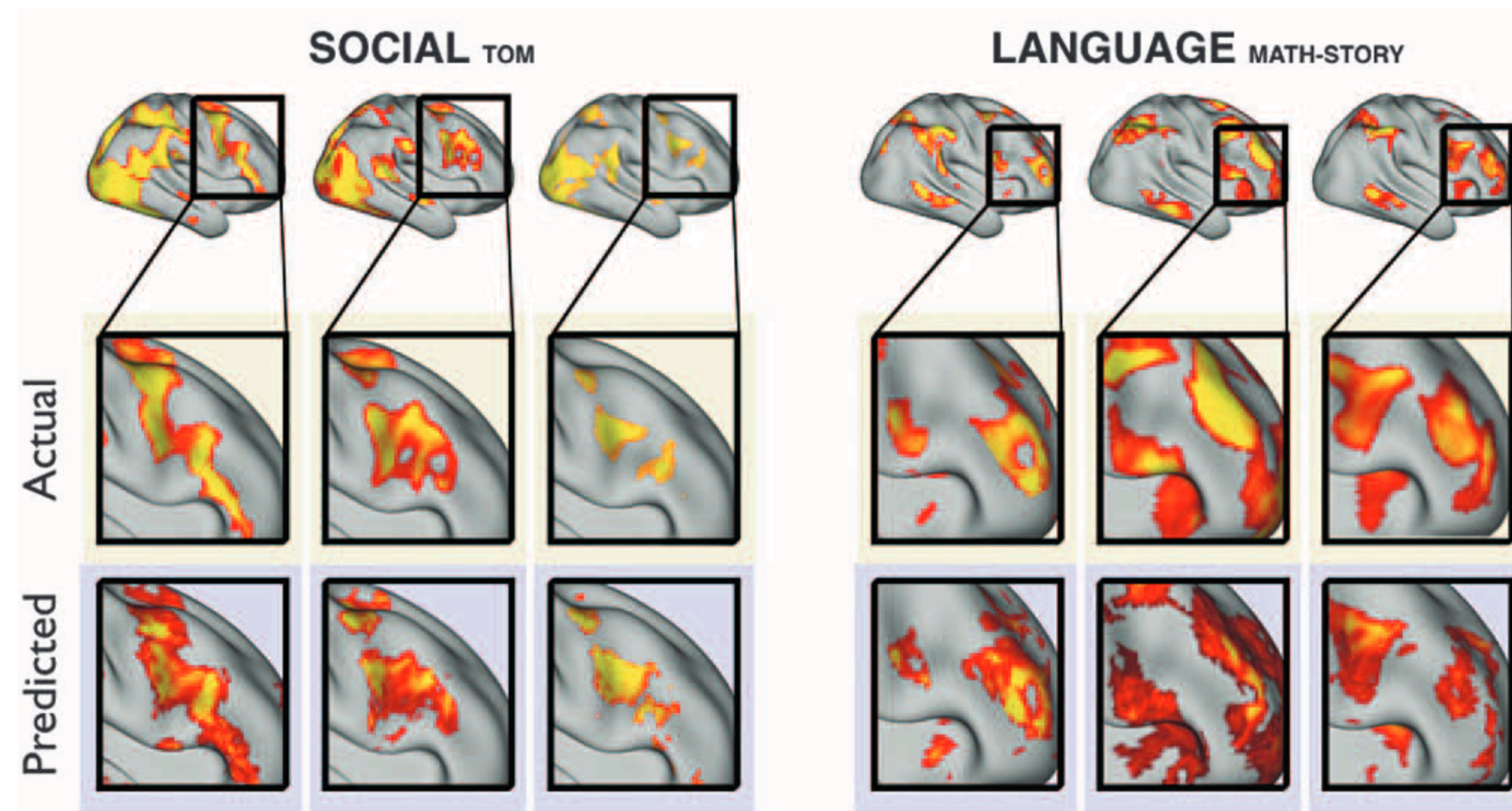
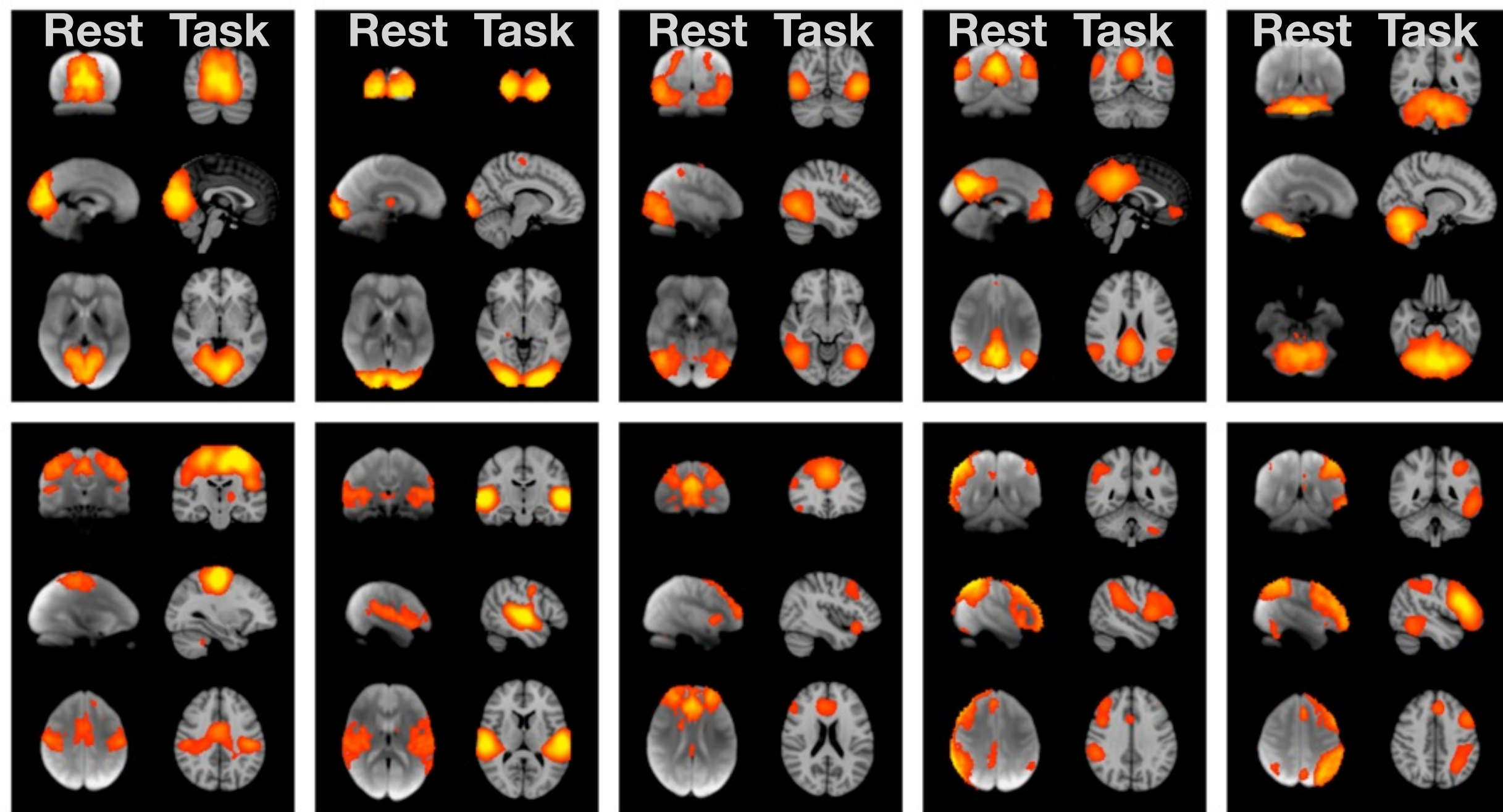
静息态网络结构位于灰质内



Relationship to task 与任务的关系

Resting state networks are similar to task activation patterns at group and single subject level

静息态网络类似于组和单个被试的任务激活模式

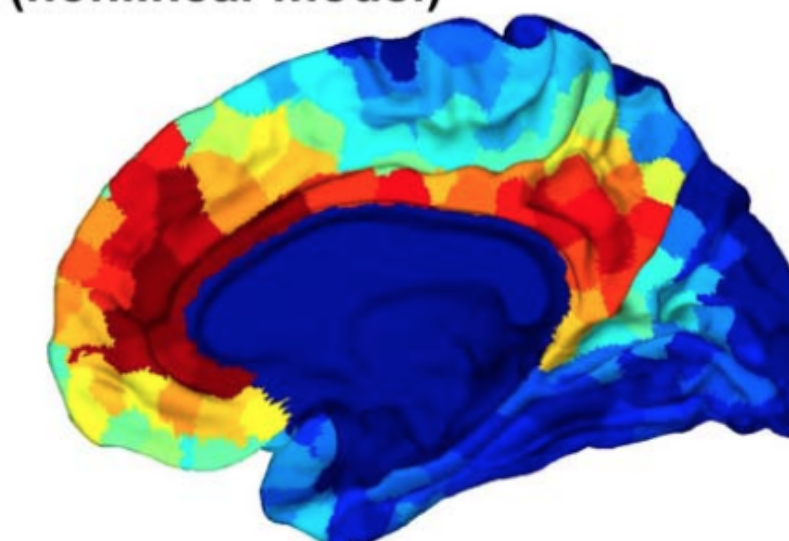
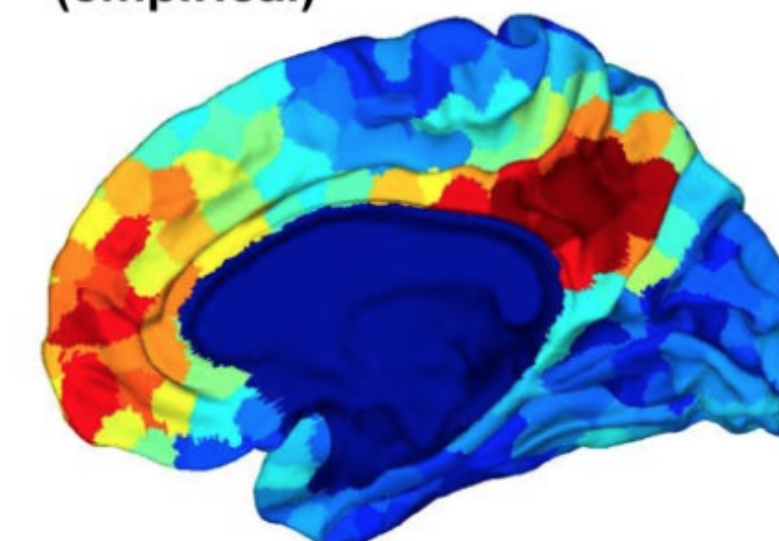
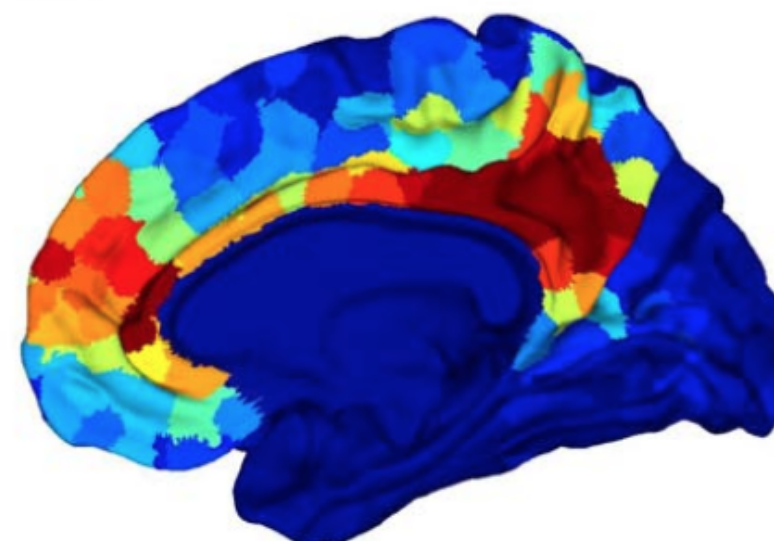
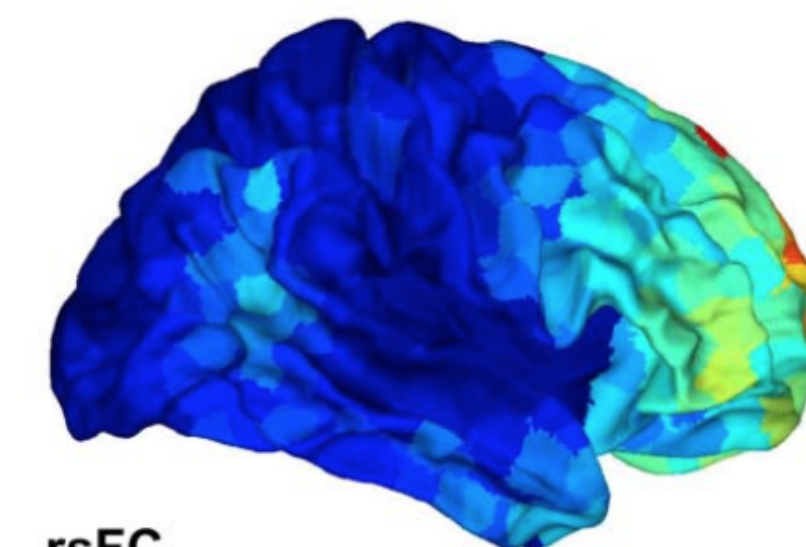
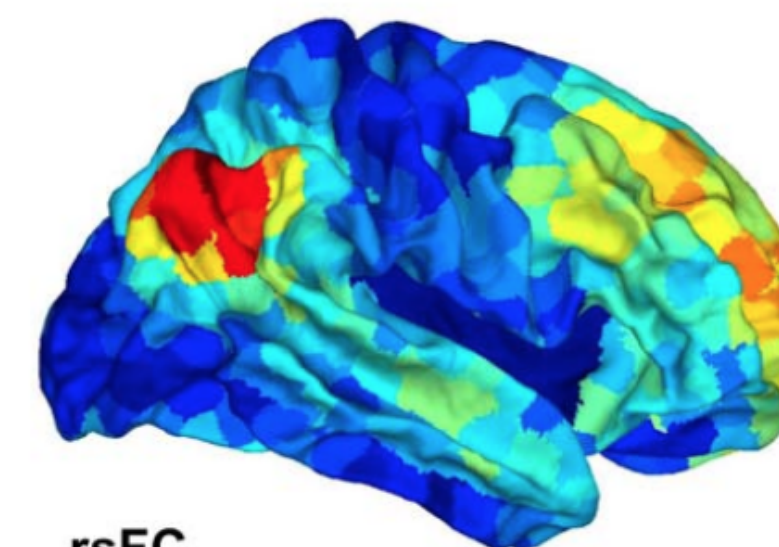
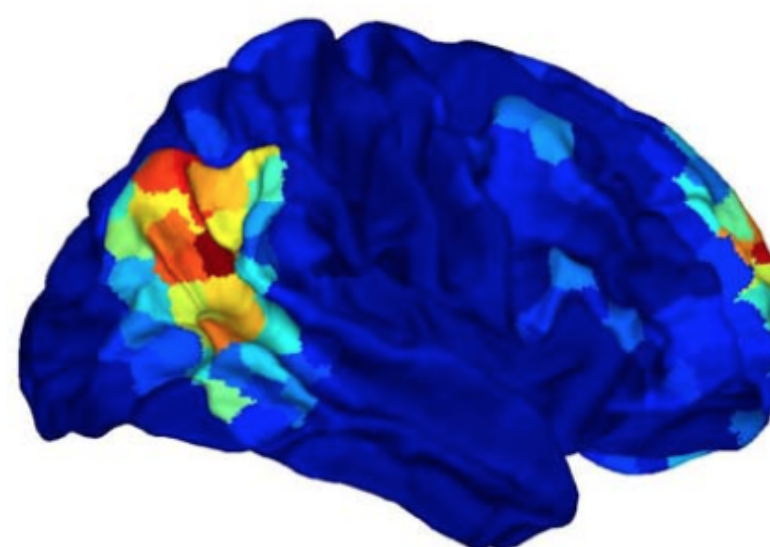
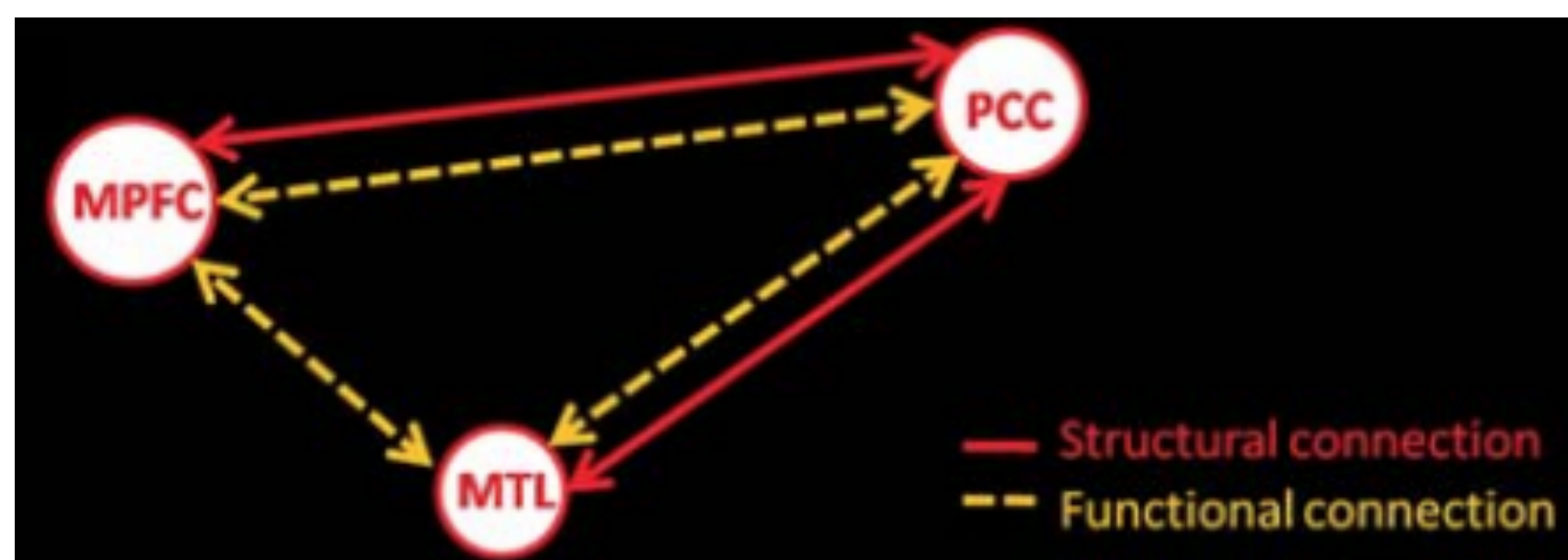
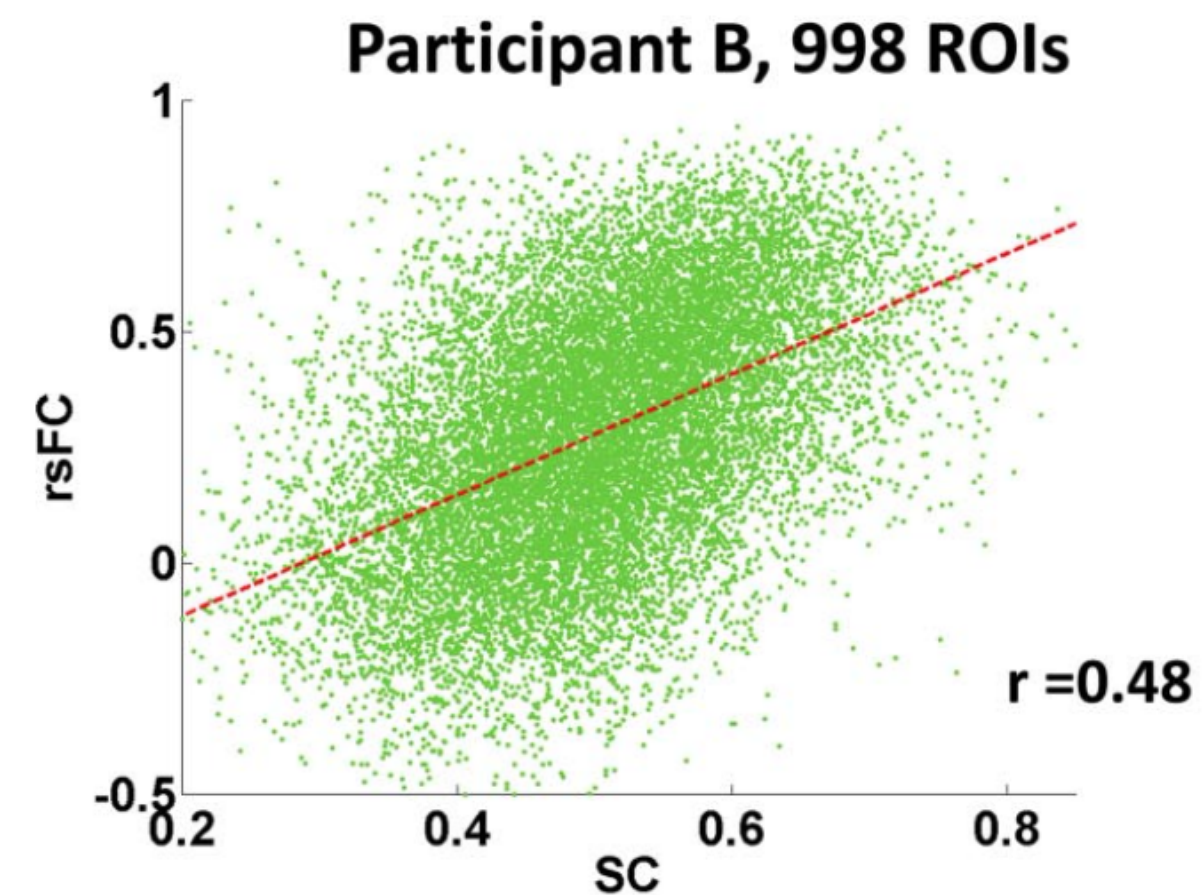


Functional vs structural connectivity

功能和结构连接

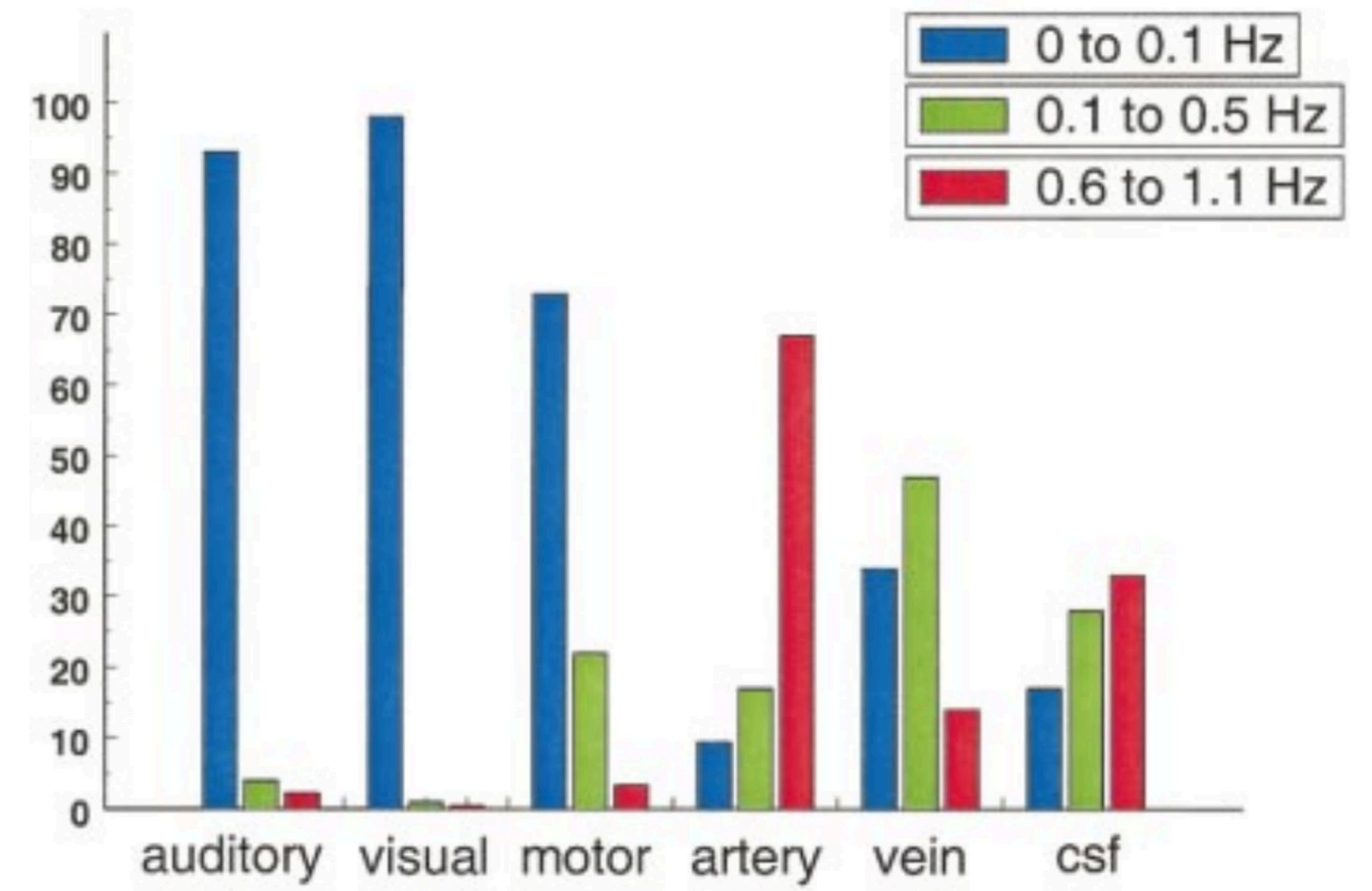
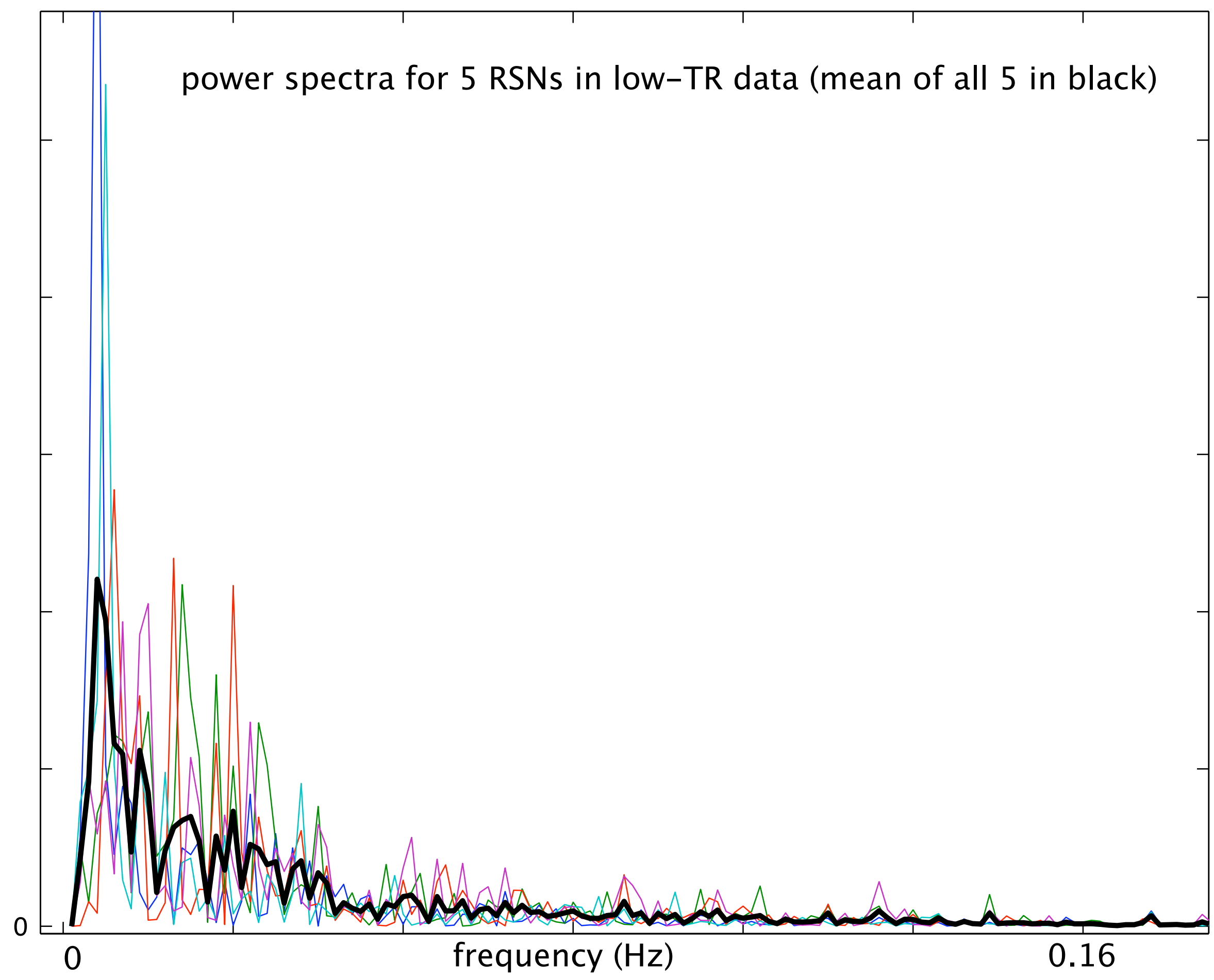
Functional connectivity is related to structural connectivity

功能连接与结构连接有关



Low frequency fluctuations?

低频波动振幅?





Low frequency fluctuations?

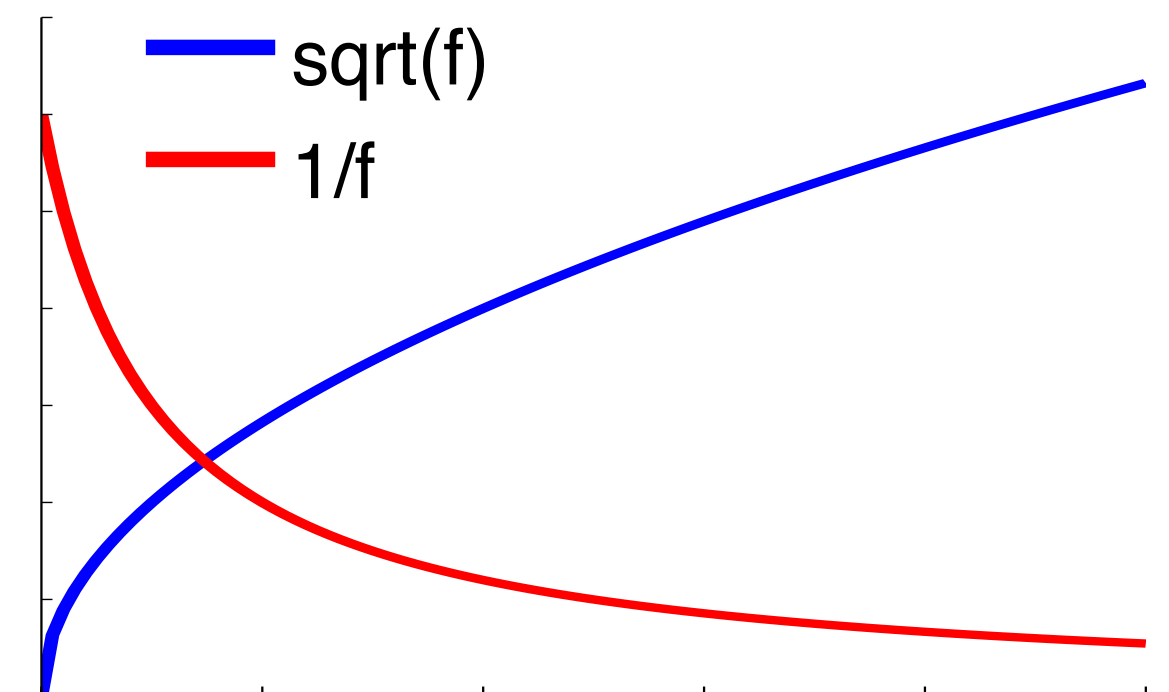
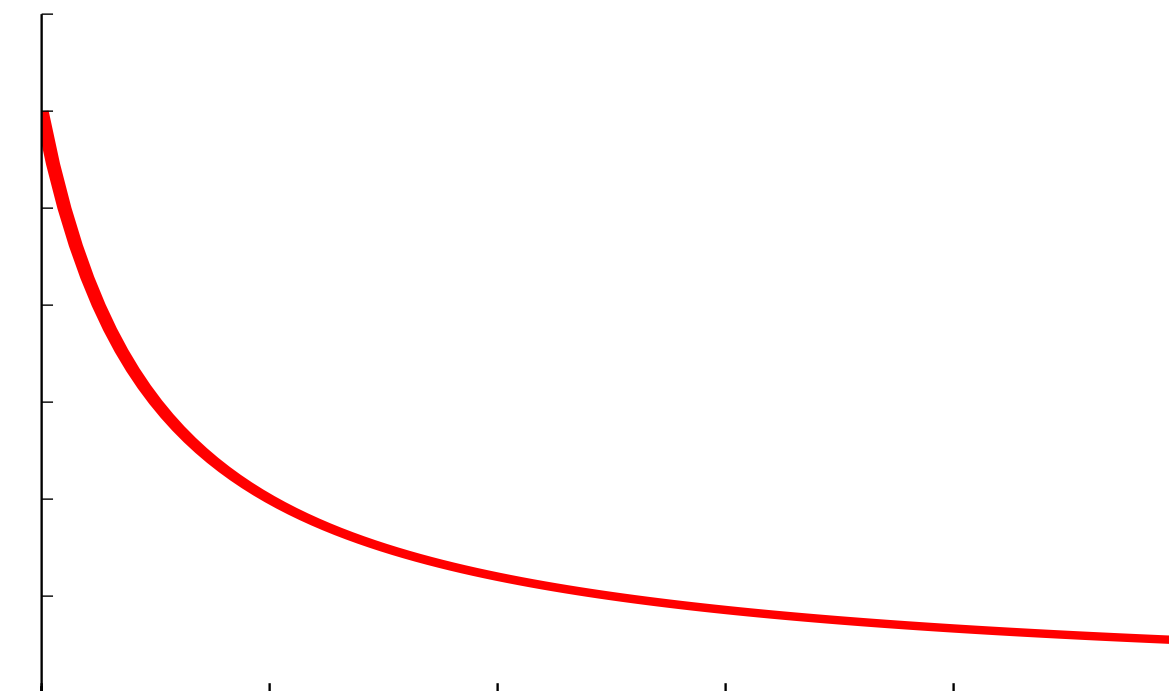
低频波动振幅?

- BOLD decreases as $1/f$

*BOLD*降低 $1/f$

- Degrees of freedom increase as $\text{sqrt}(f)$

自由度增加为 $\text{sqrt}(f)$





Low frequency fluctuations?

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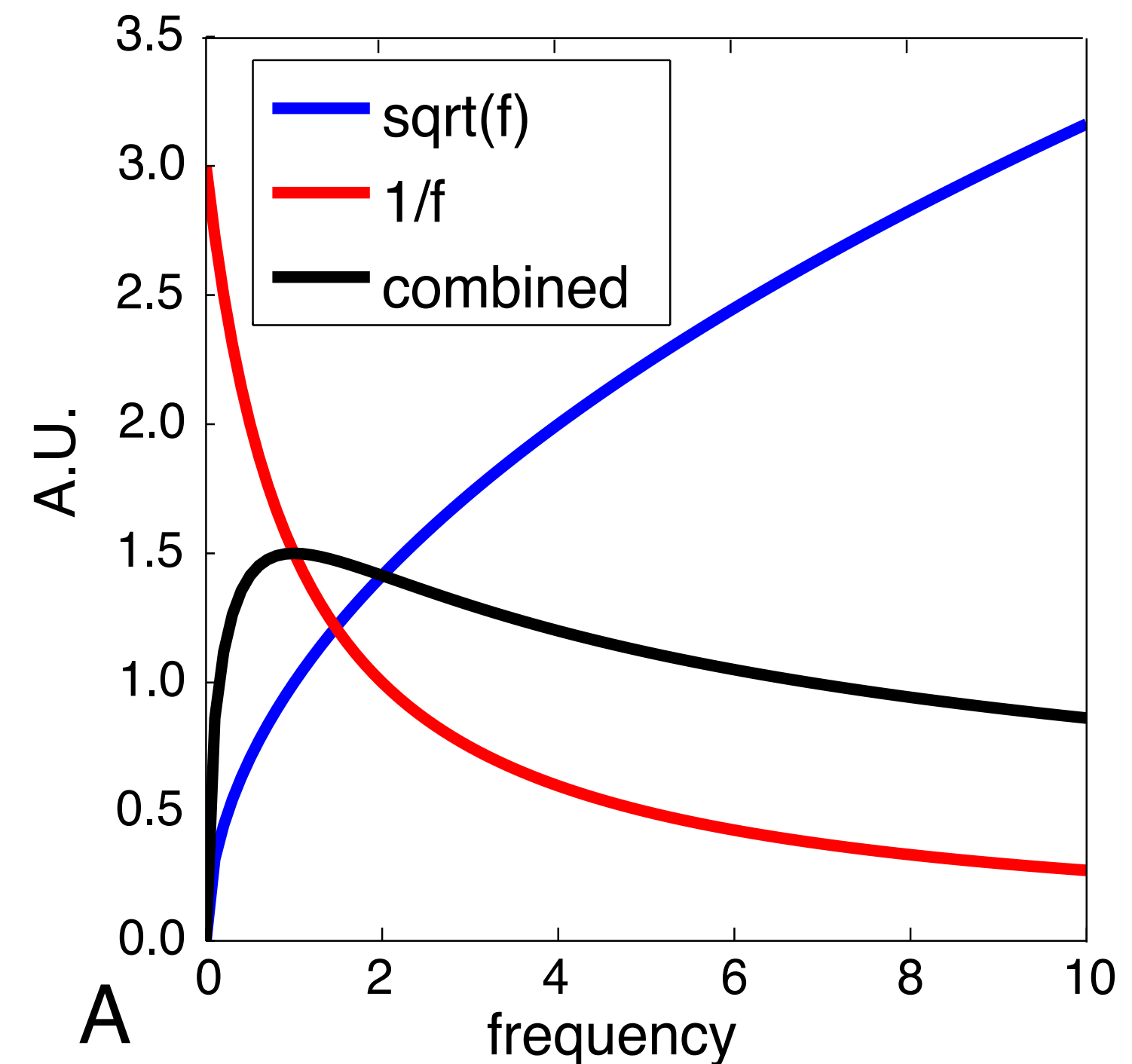
BOLD降低 $1/f$

- Degrees of freedom increase as $\text{sqrt}(f)$

自由度增加为 $\text{sqrt}(f)$

- Combined effect contributes to RSN estimation across frequency range!

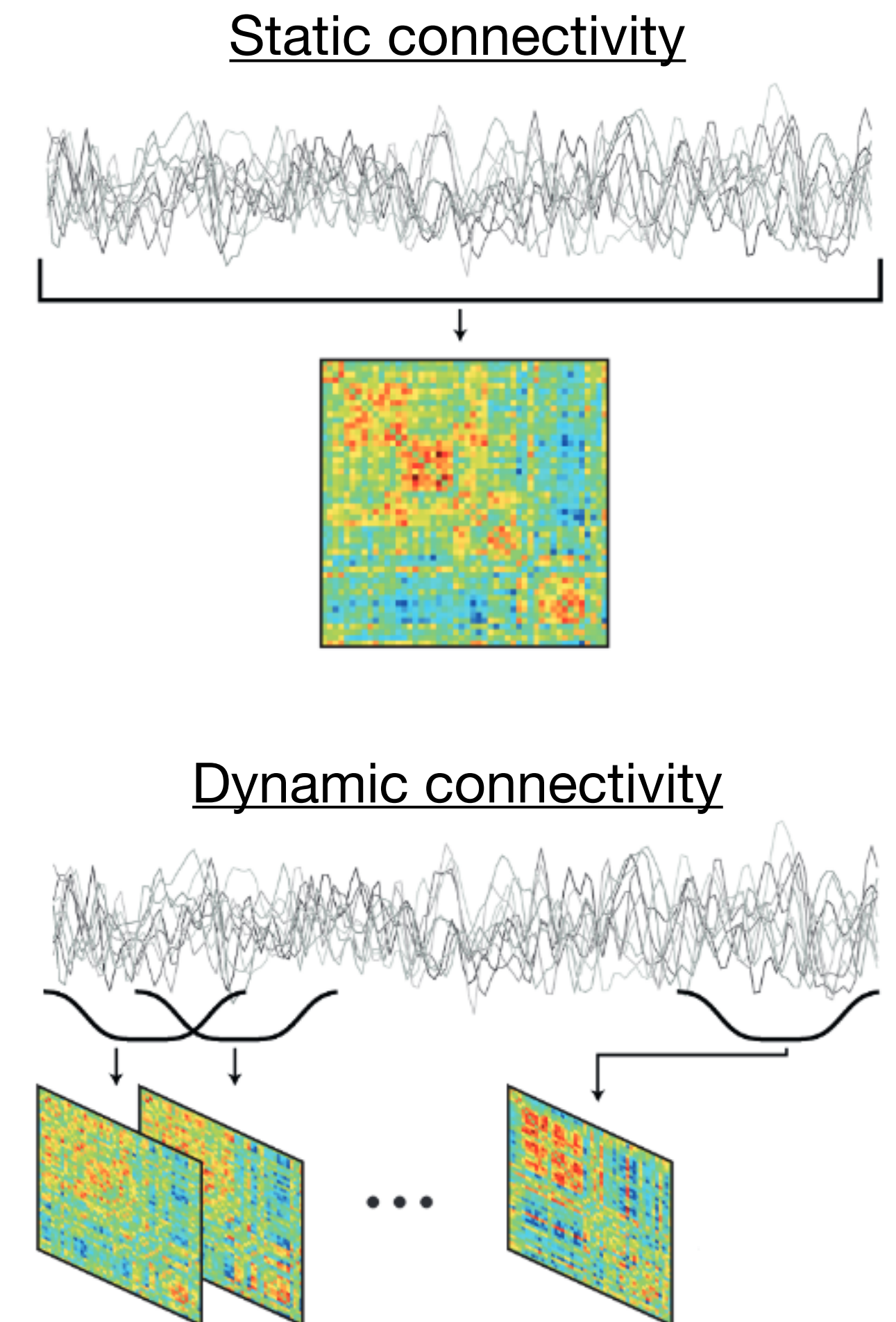
联合效应有助于跨频率范围的RSN估计!



Static versus dynamic connectivity

静态与动态连接

- Most connectivity measures are static (based on the full resting state scan) 大多数连接度量是静态的（基于完全静止状态扫描）
- Dynamic connectivity is like to occur (changes over time) 动态连接似乎会发生（随时间变化）
- Static connectivity measures reflect average across dynamic states 静态连接度量反映了动态的平均值
- Dynamic connectivity measures are challenging (in terms of noise influences, significance testing) 动态连接测量具有挑战性（在噪声和显著性检验方面）



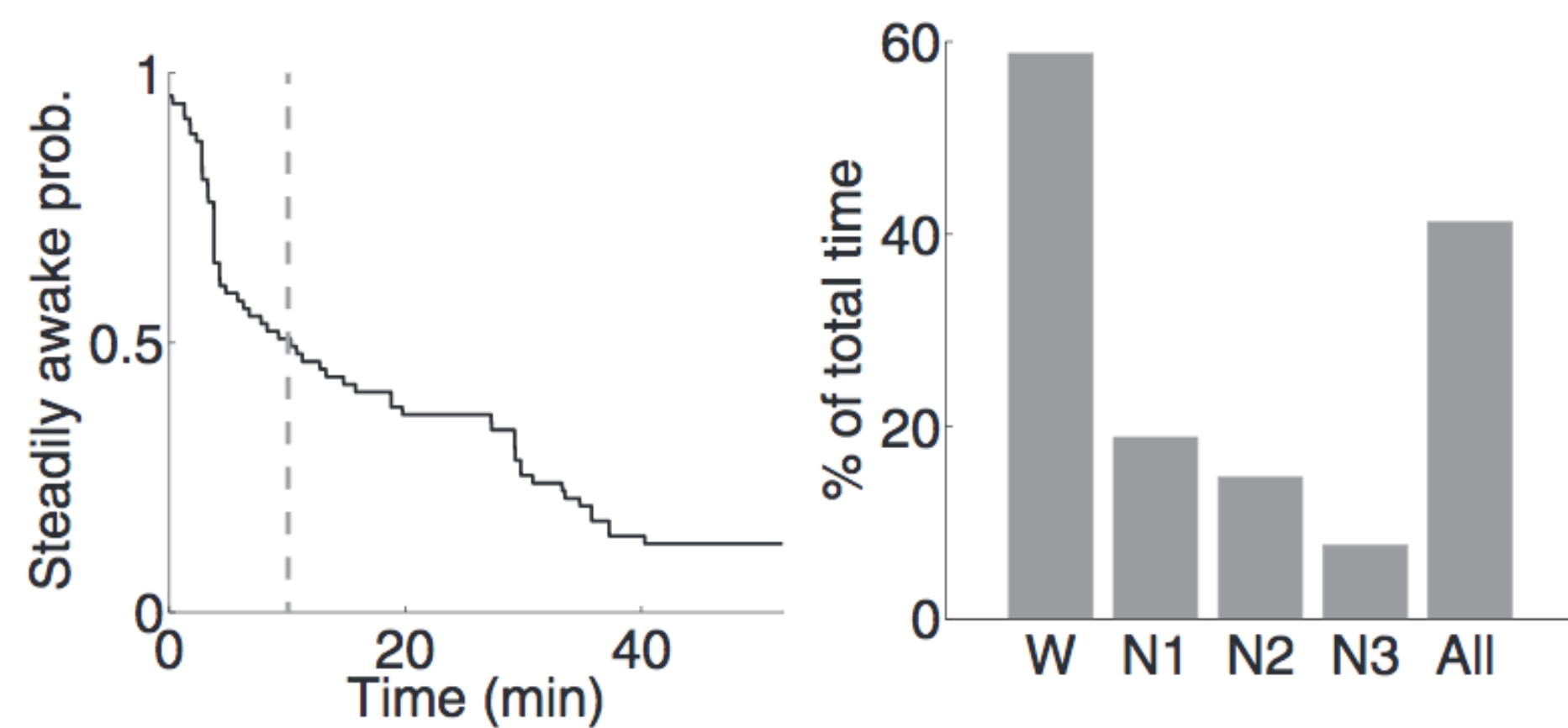


Arousal 觉醒

- Subjects fall asleep 受试者入睡

Arousal 觉醒

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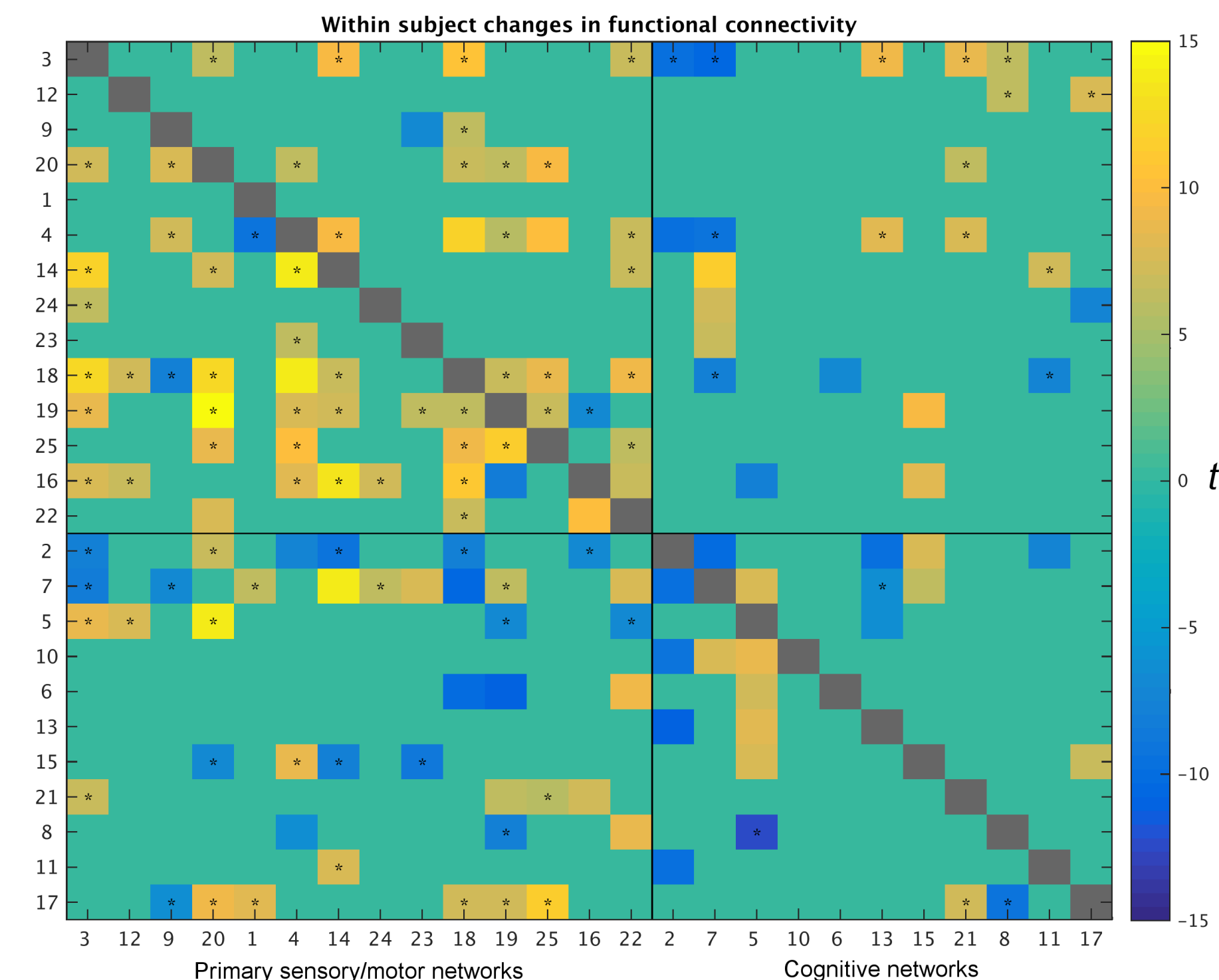
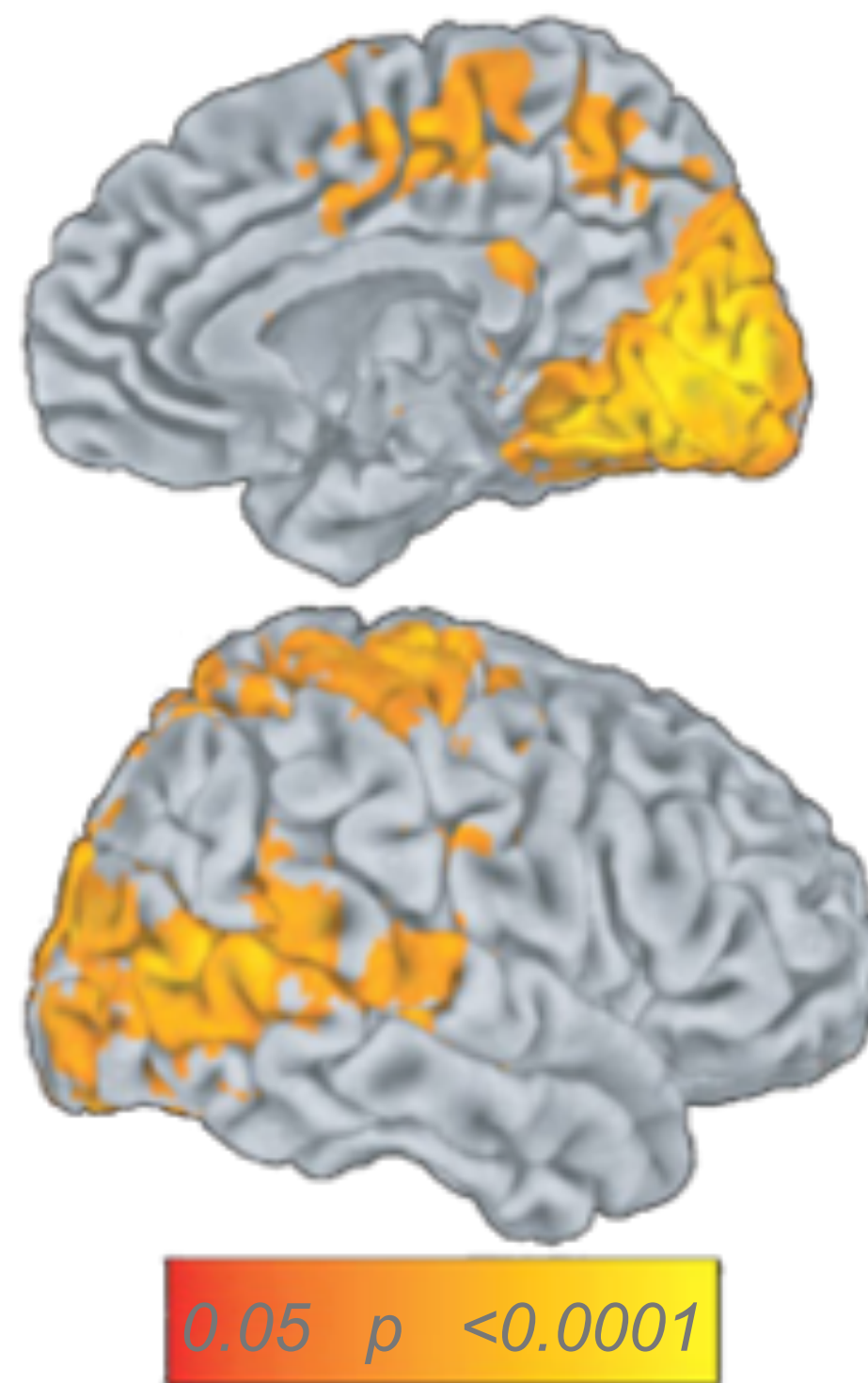
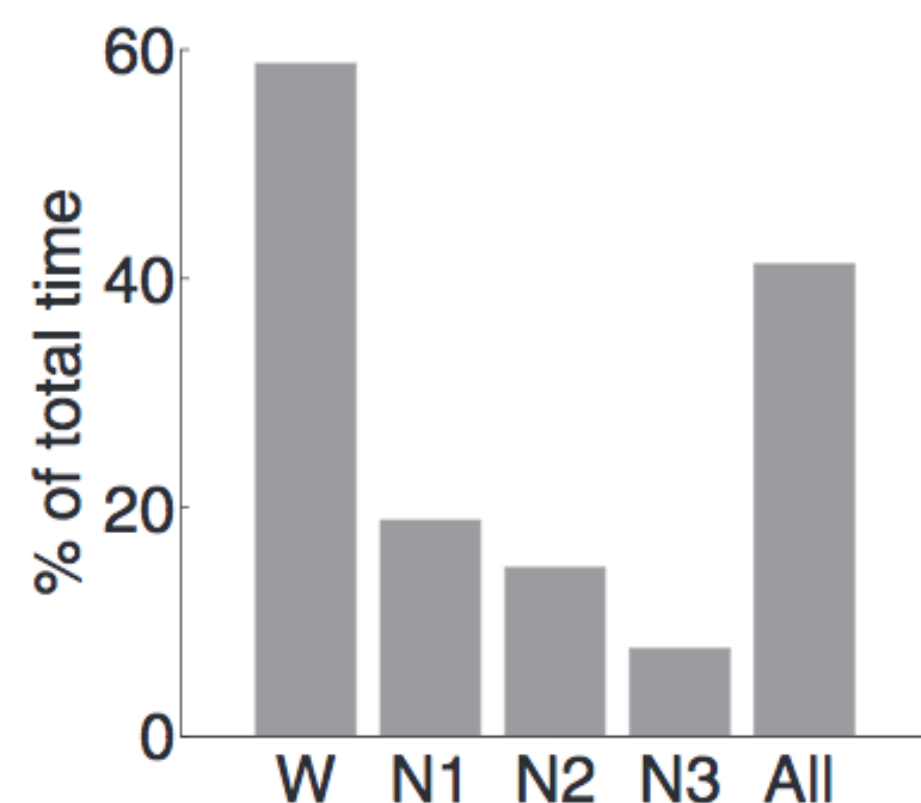
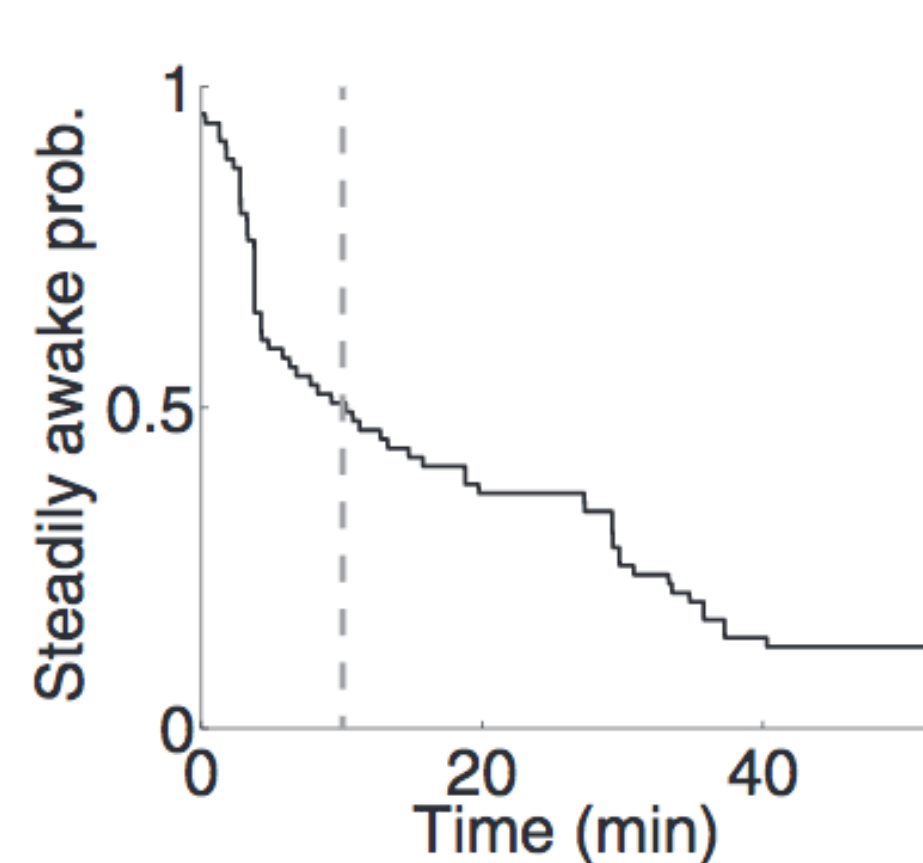


Arousal 觉醒

- Subjects fall asleep 受试者入睡

- Changes in BOLD amplitude
BOLD幅度的变化

- Related changes in correlation
相关性变化





Preprocessing

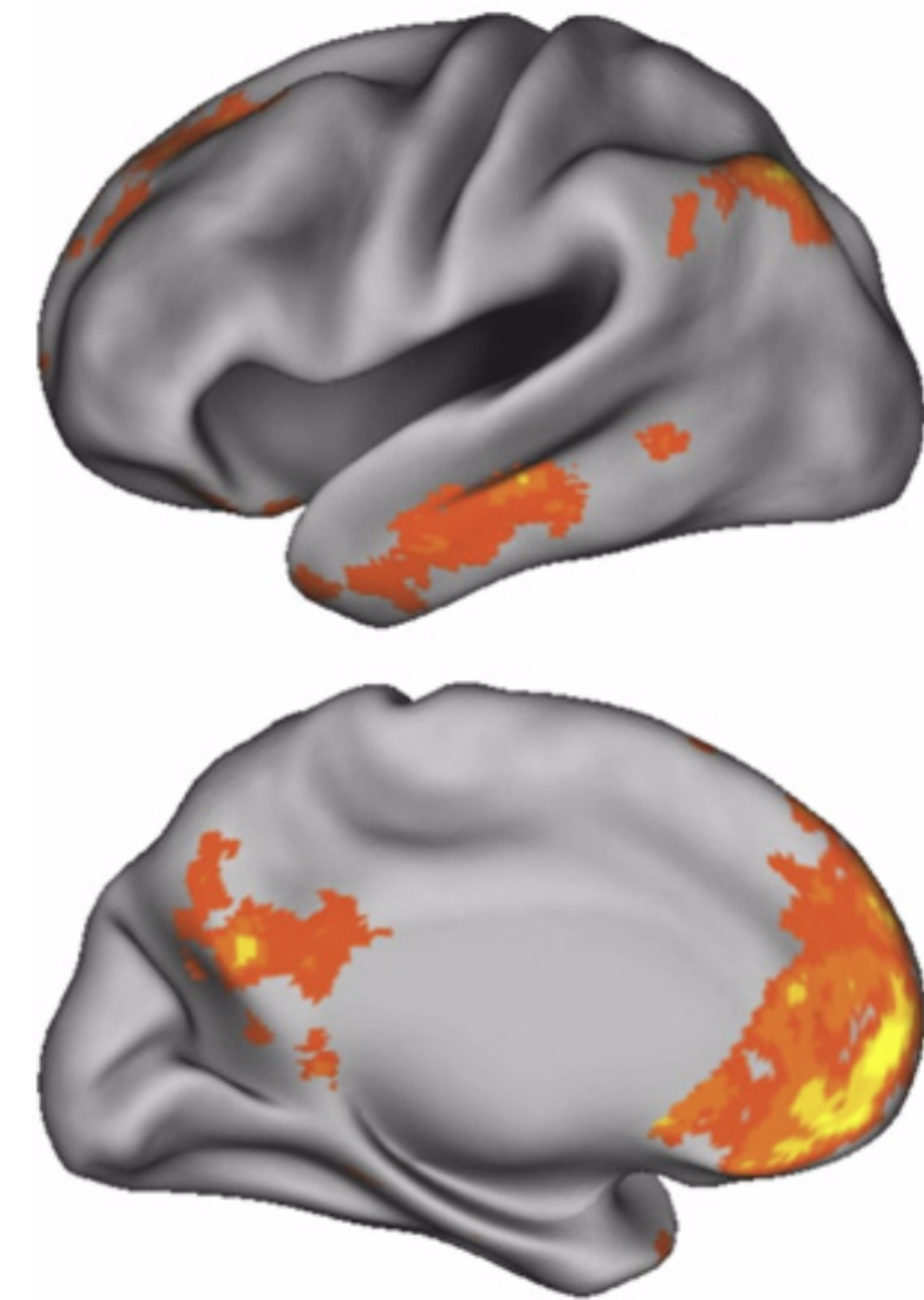
预处理

Careful cleanup required

需要仔细去噪

- Structured artefacts much more of a problem for rfMRI than task-fMRI rfMRI比task-fMRI存在更多的人工因素
- No model of expected activation 没有预期激活的模型
- Instead based on correlating timeseries with each other 而是基于将时间序列相互关联

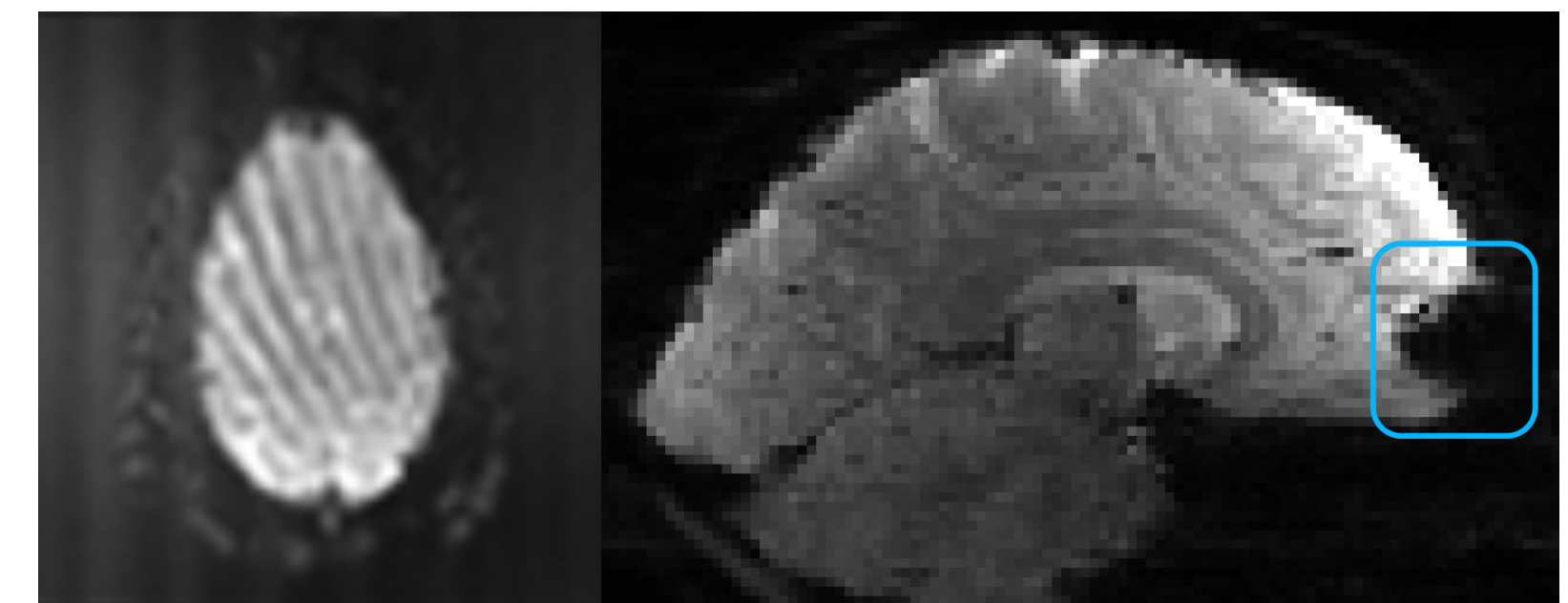
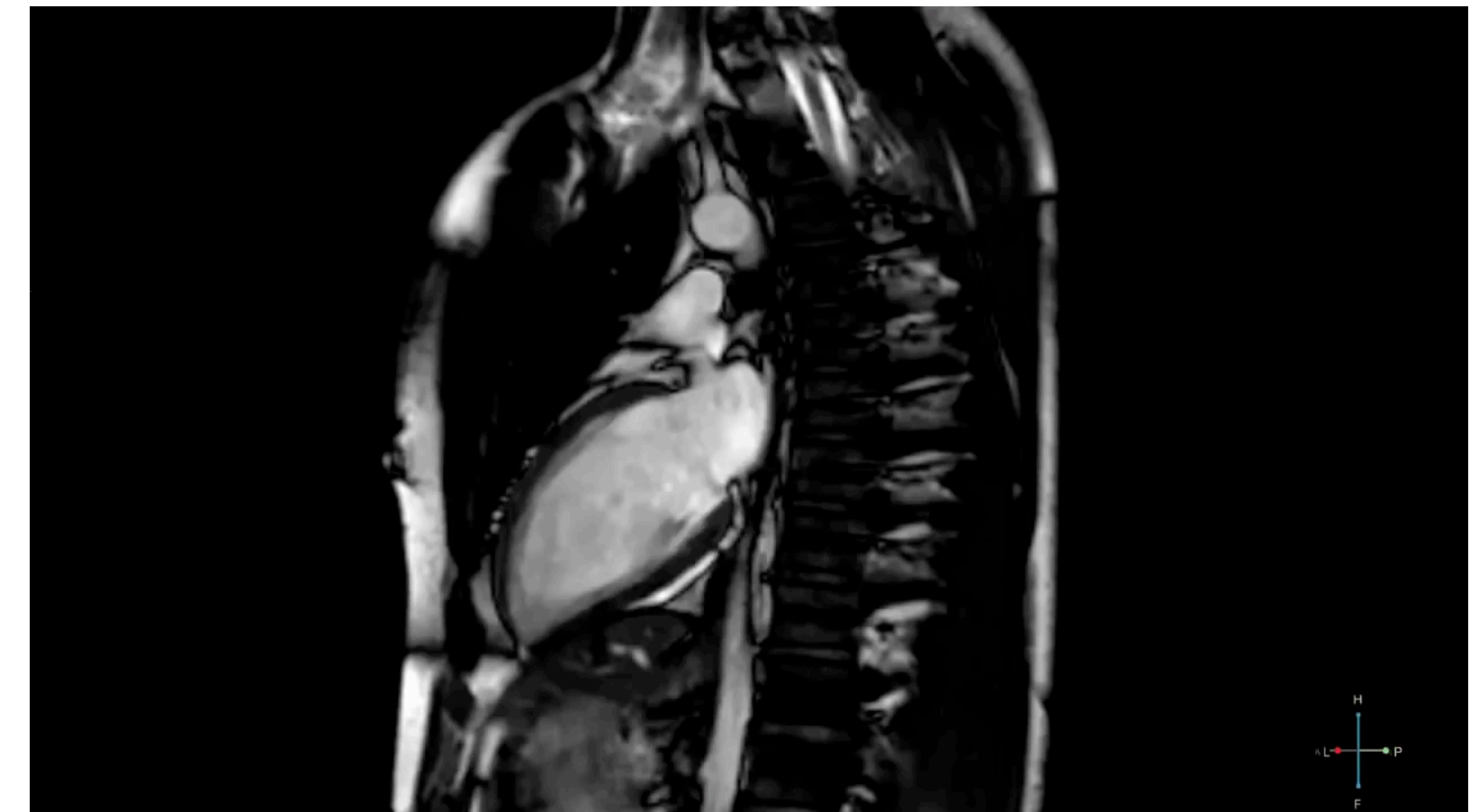
Low motion > high motion



Noise sources

噪声来源

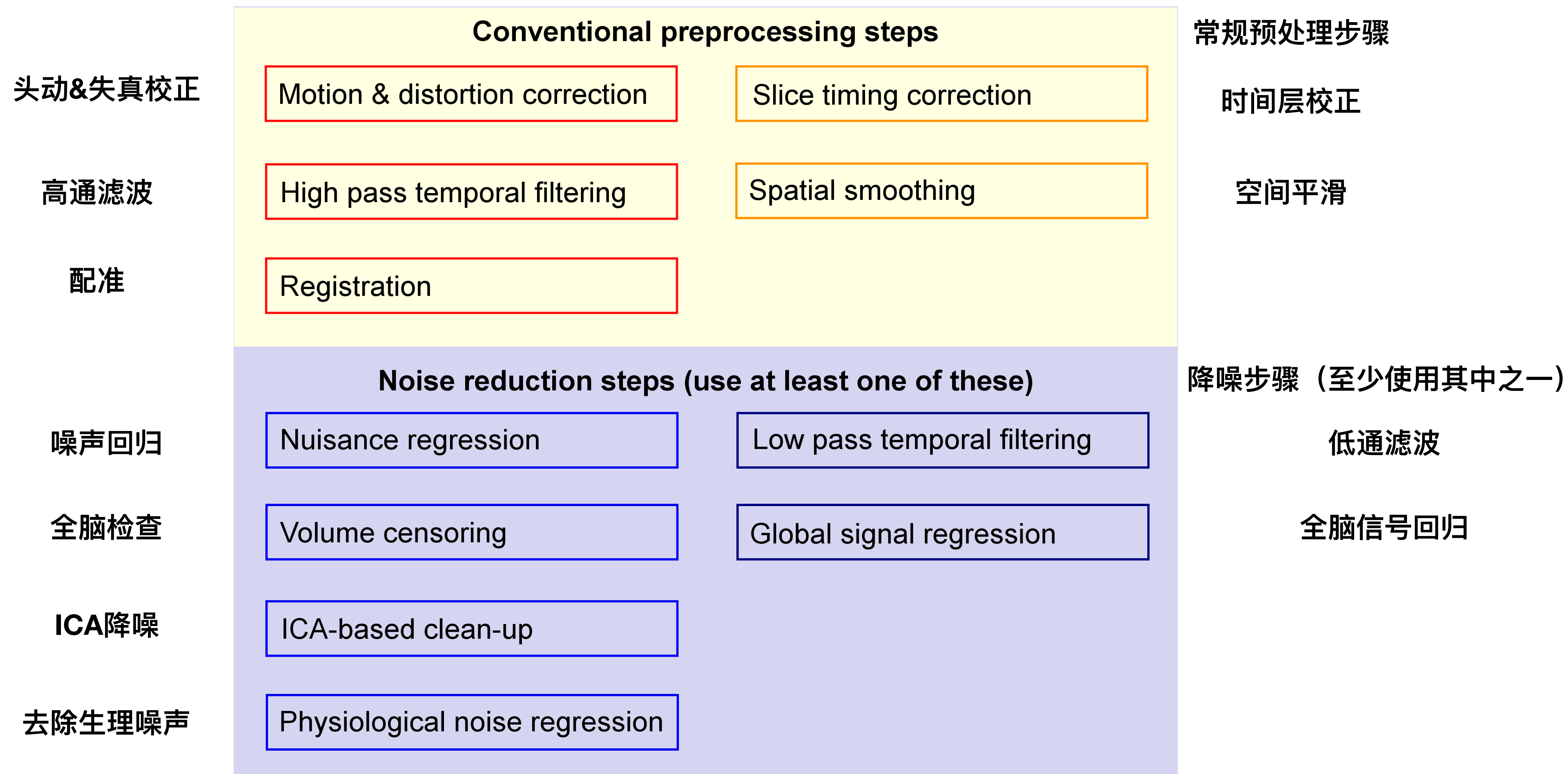
- Head motion 头动
- Cardiac & breathing cycles 心跳和呼吸周期
- Scanner artefacts 扫描仪噪声





Preprocessing overview

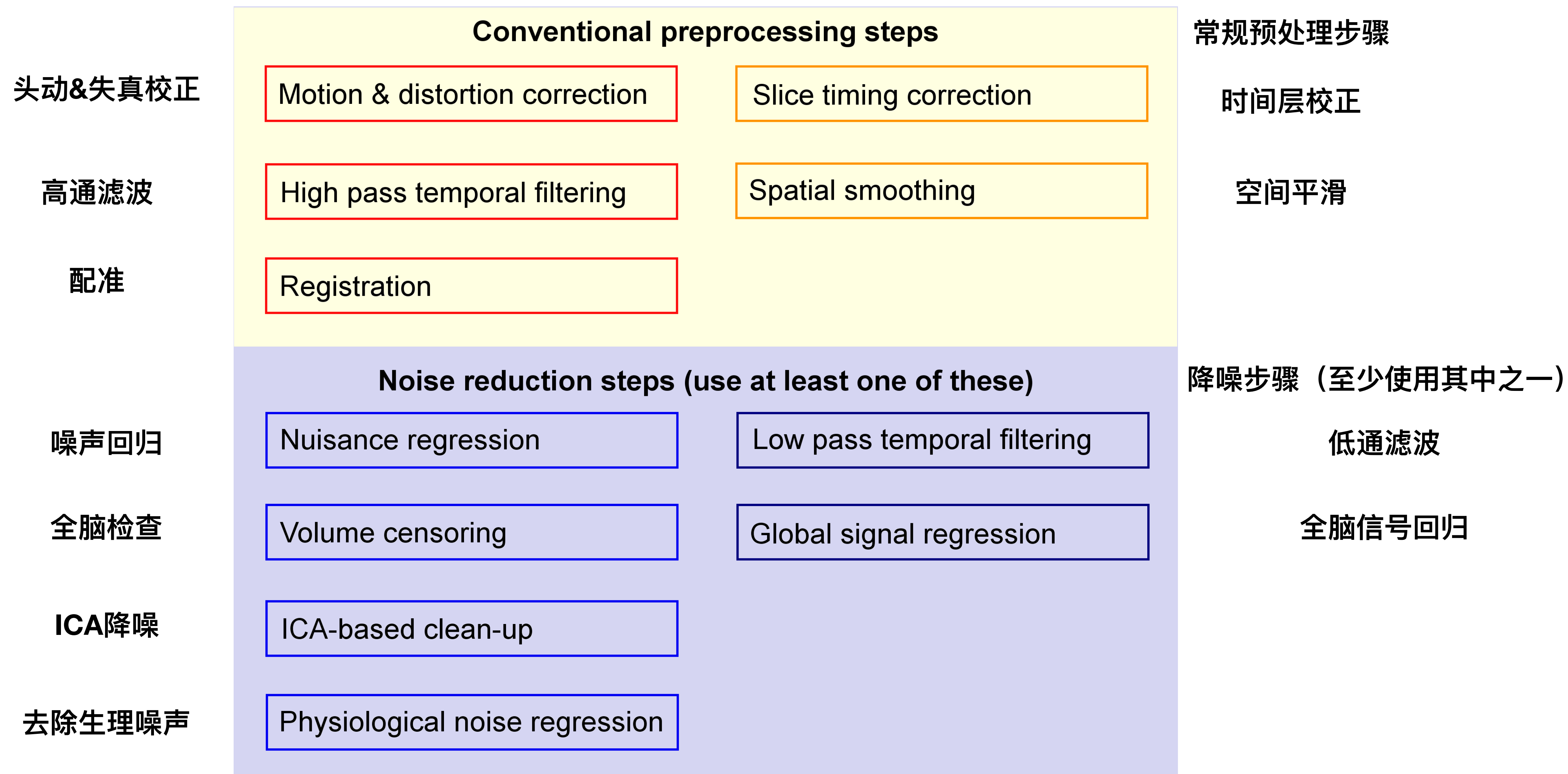
预处理概述





Preprocessing overview

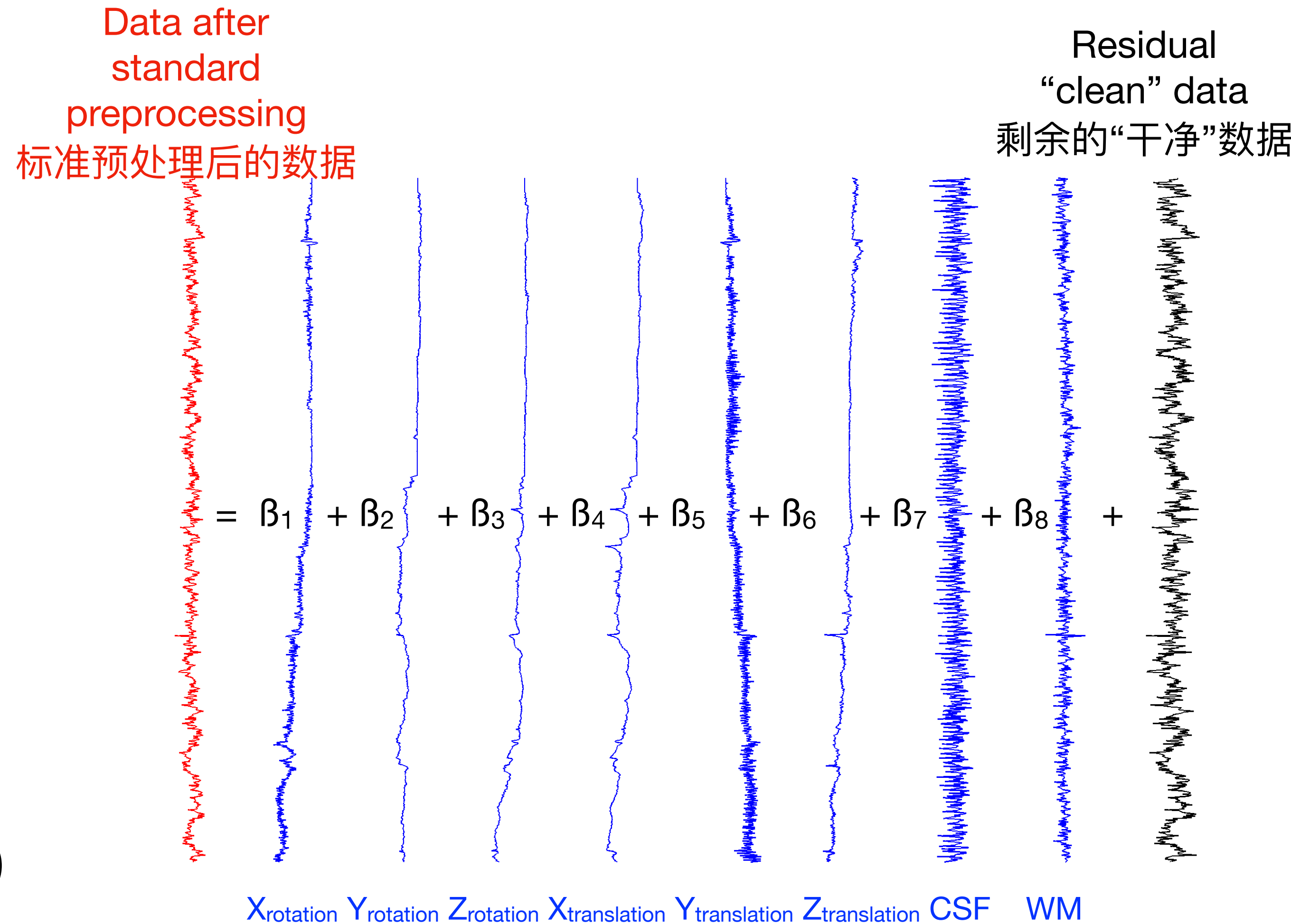
预处理概述



Nuisance regression

噪声回归

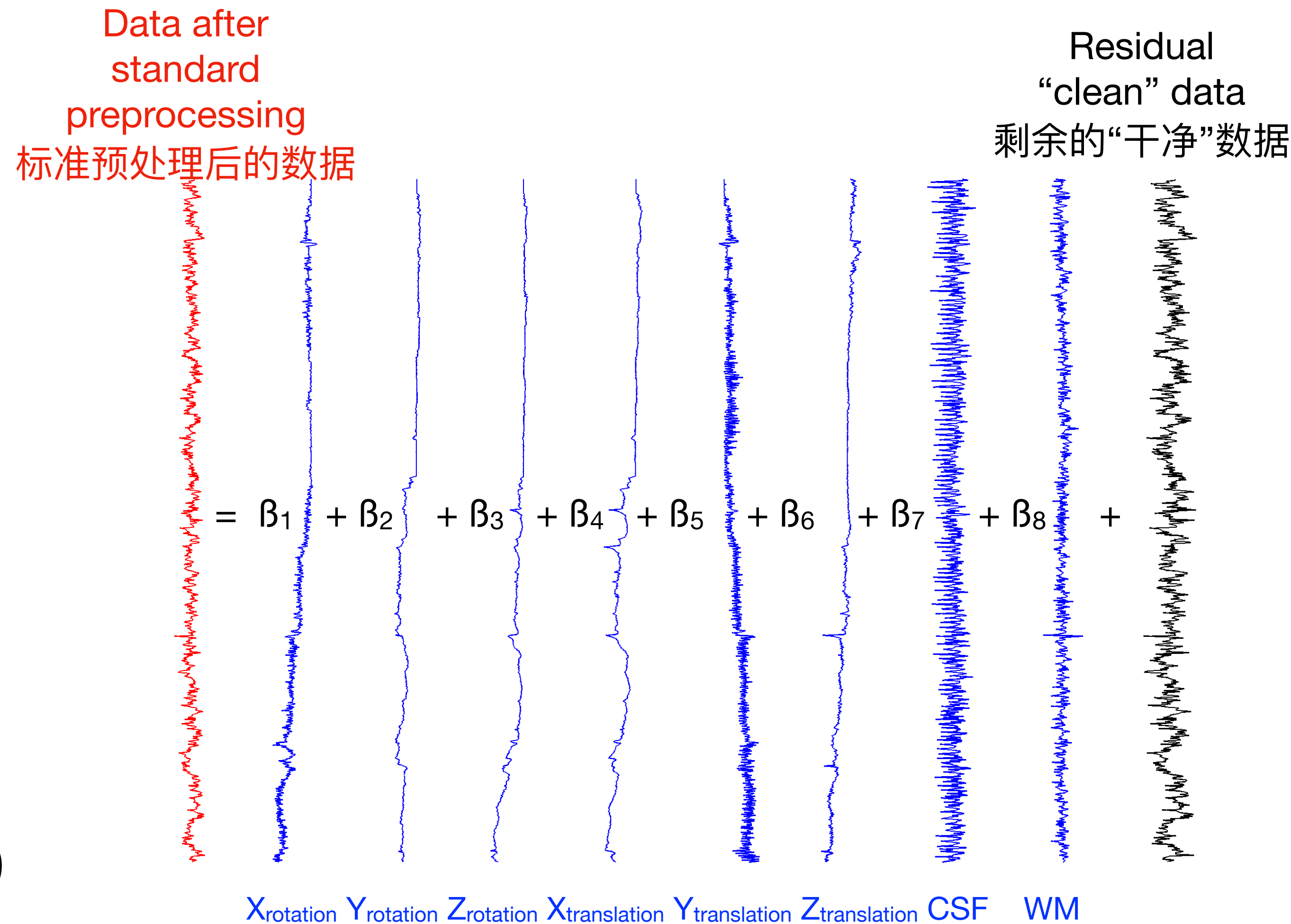
- Head motion parameters (头动参数)
- White-matter / CSF (白质/脑脊液)
- Use GLM to remove nuisance timeseries (GLM去除噪声时间序列)
- Perform analysis on residuals (残差分析)
- “CompCor” method (PCA-based) (“CompCor”方法 (基于PCA))



Nuisance regression

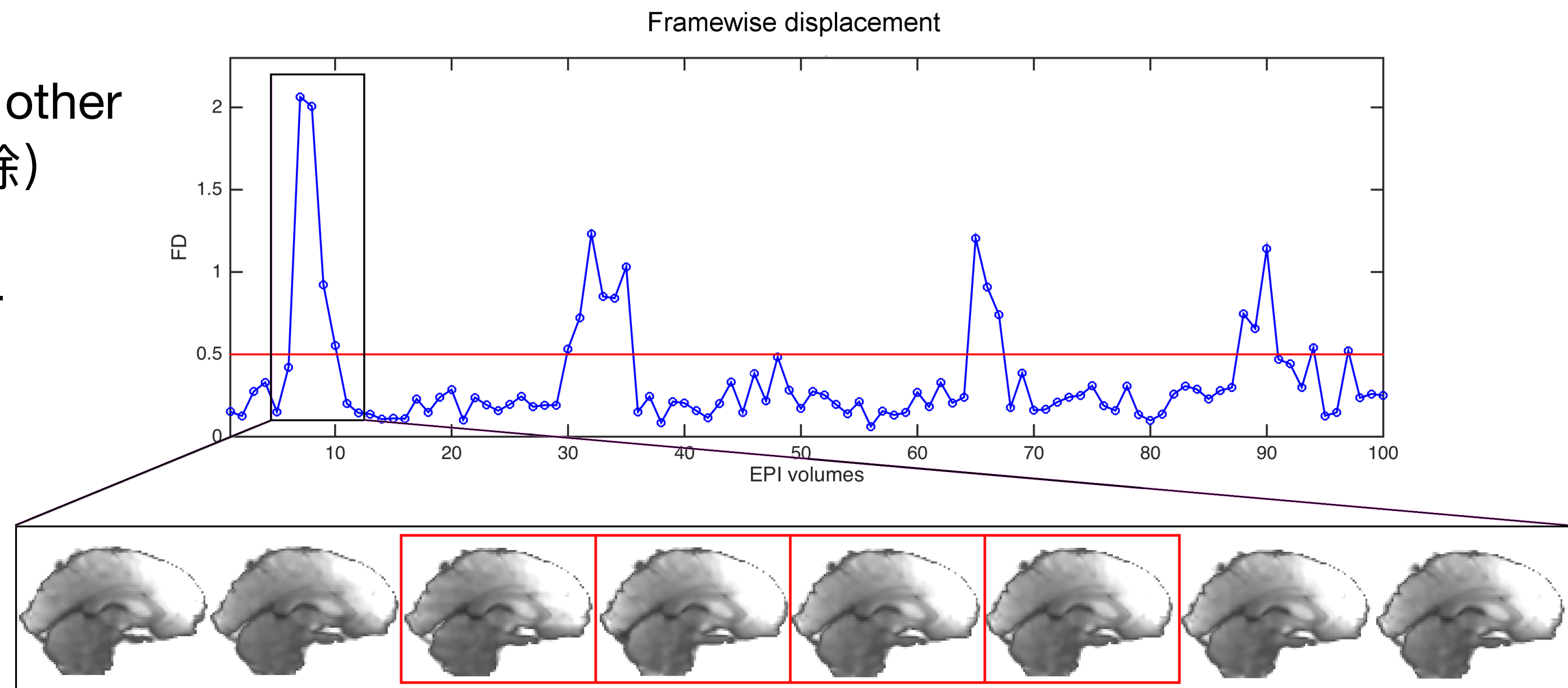
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Volume censoring 大脑检查

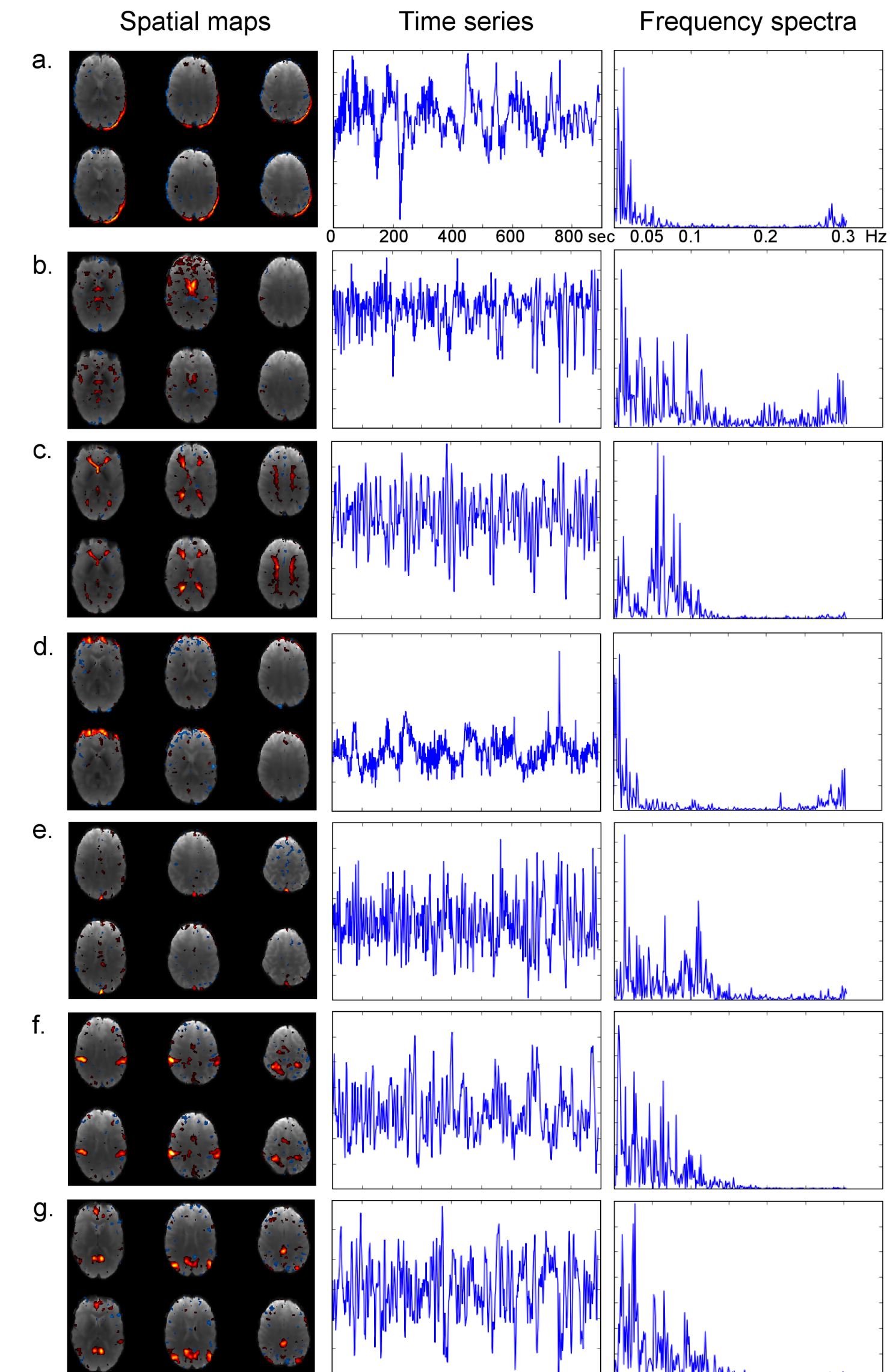
- Remove volumes with high motion (移除头动较大的图像)
- Very effective to fully remove large motion effects (移除头动较大的体素效果很好)
- But, does not remove small motion effects and other noise sources (头动小的以及其他噪声不要移除)
- Also known as scrubbing, spike regression, de-spiking
也称为去噪, 尖峰回归, 去尖峰



ICA based cleanup

ICA降噪

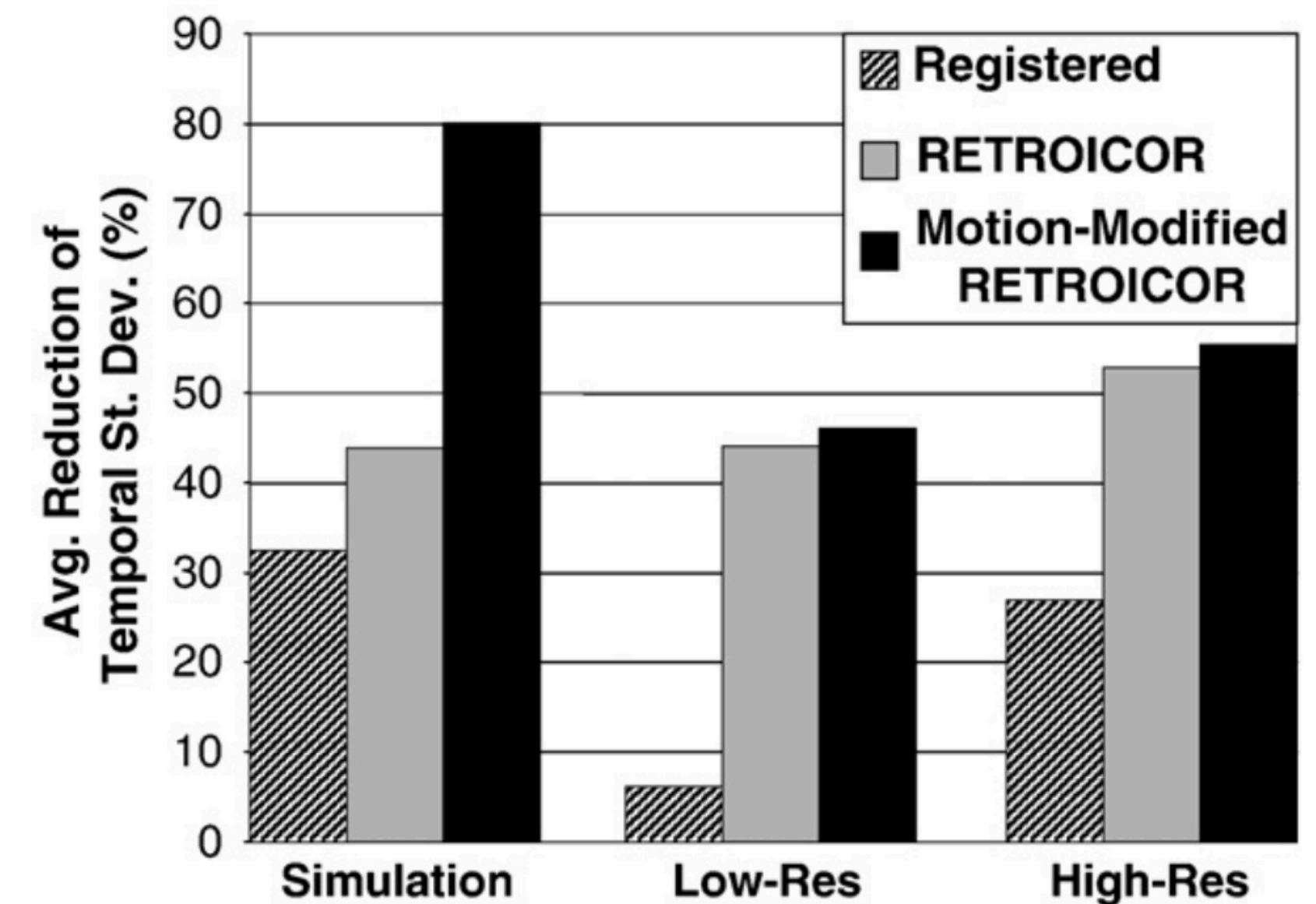
- Semi-Automatic labelling methods available (ICA-FIX, ICA-AROMA)
半自动标记的方法 (ICA-FIX, ICA-AROMA)
- Removes most types of artefacts (motion, physiology, scanner)
删除大多数类型的噪声 (头动、生理、扫描设备)
- But, does not capture global (spatially extended) noise
但是, 不会删除全局 (空间扩展) 噪声



Physiological noise regression

去除生理噪声

- PNM, RETROICOR
- Requires physiological measurements during scan 在扫描期间需要生理信号测量
- Generates regressors based on physiological data 基于生理数据生成回归量

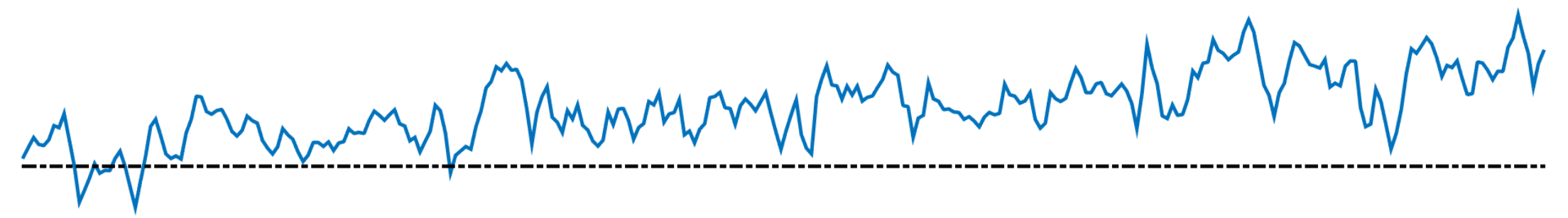


Lowpass temporal filtering

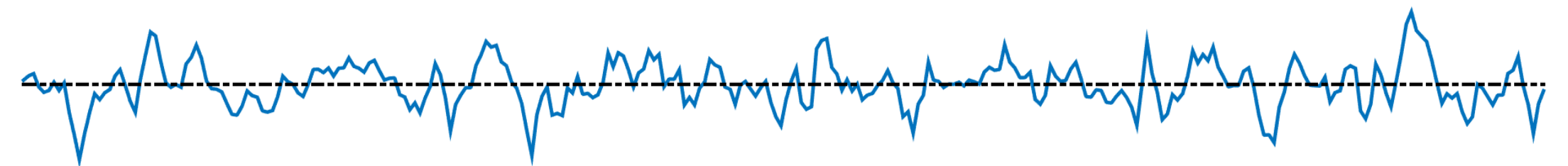
低通时间滤波

- E.g., common to remove frequencies $> 0.1\text{ Hz}$
通常去除 $> 0.1\text{ Hz}$ 的频率
- May remove useful signal
可能会删除有用信号
- Not guaranteed to remove much artefact
不能保证删除很多噪声

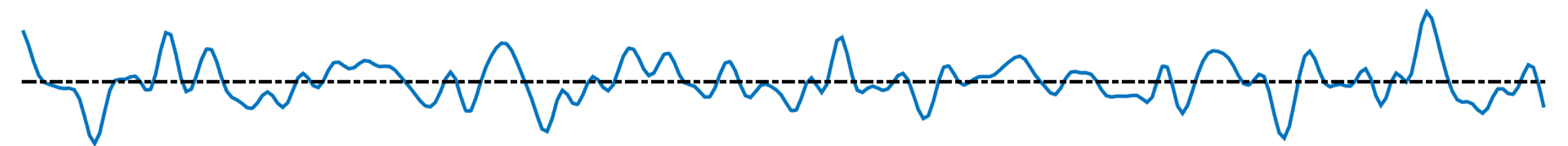
Original BOLD data



Highpass filtered data ($>0.01\text{ Hz}$)



Bandpass filtered data ($0.01 - 0.1\text{ Hz}$)

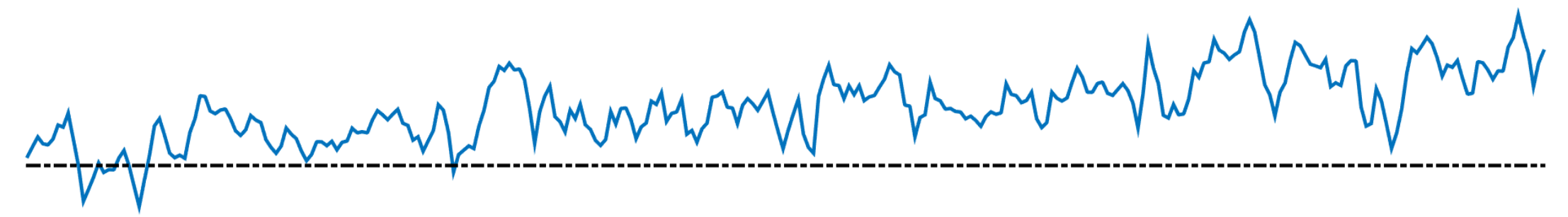


Lowpass temporal filtering

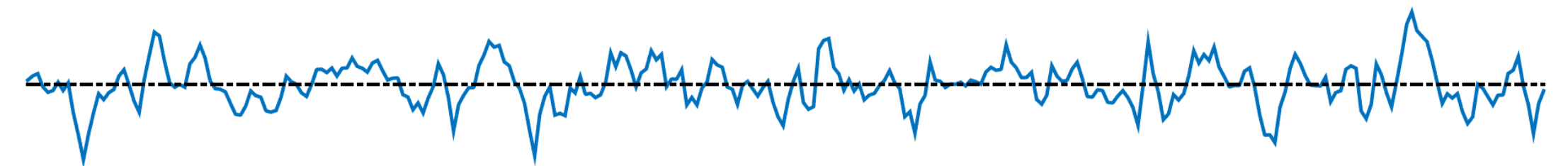
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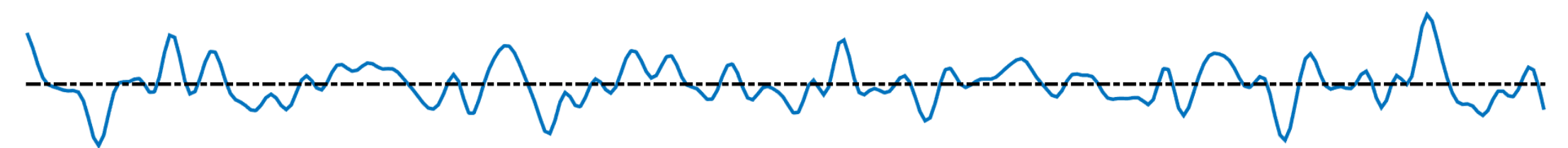
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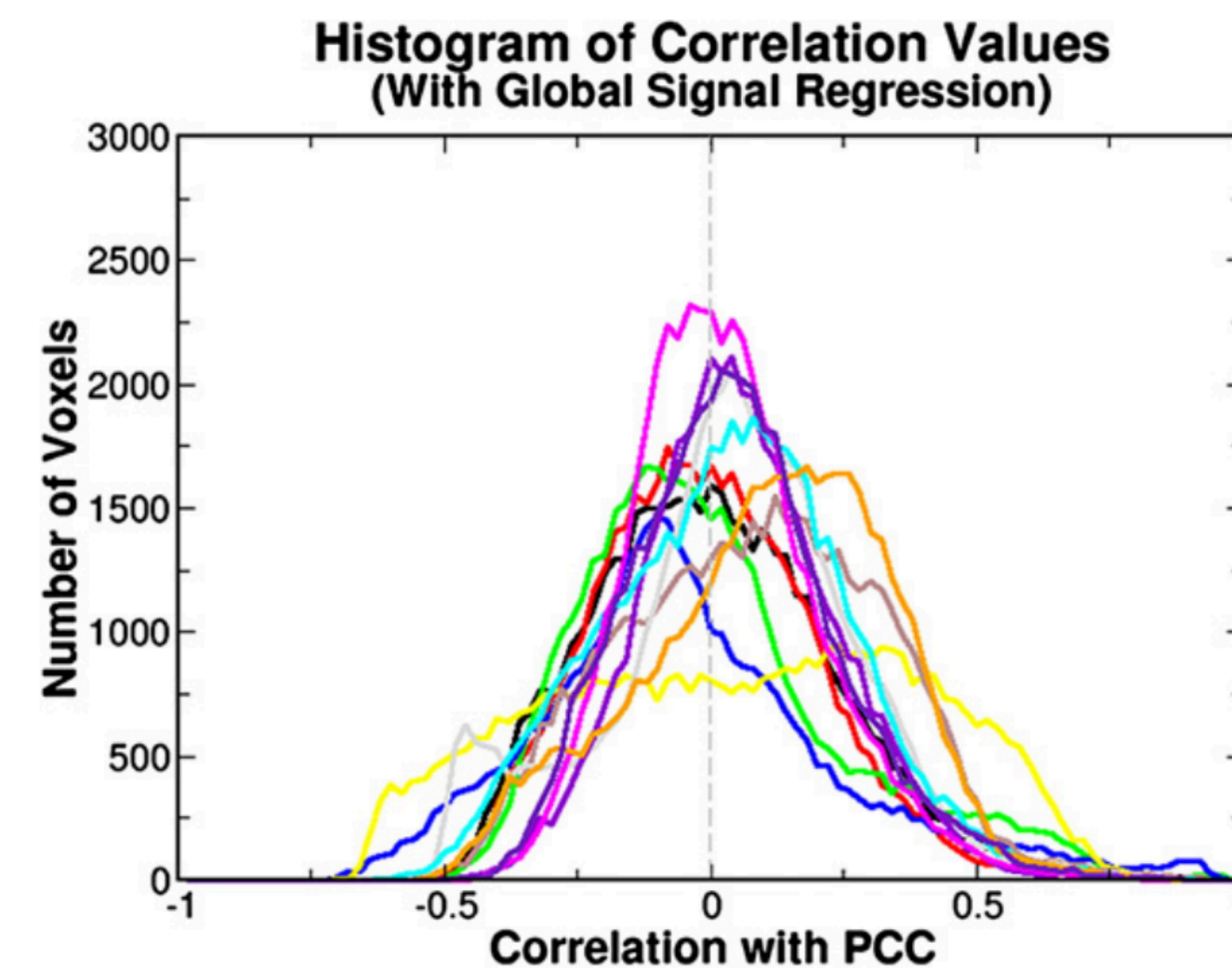
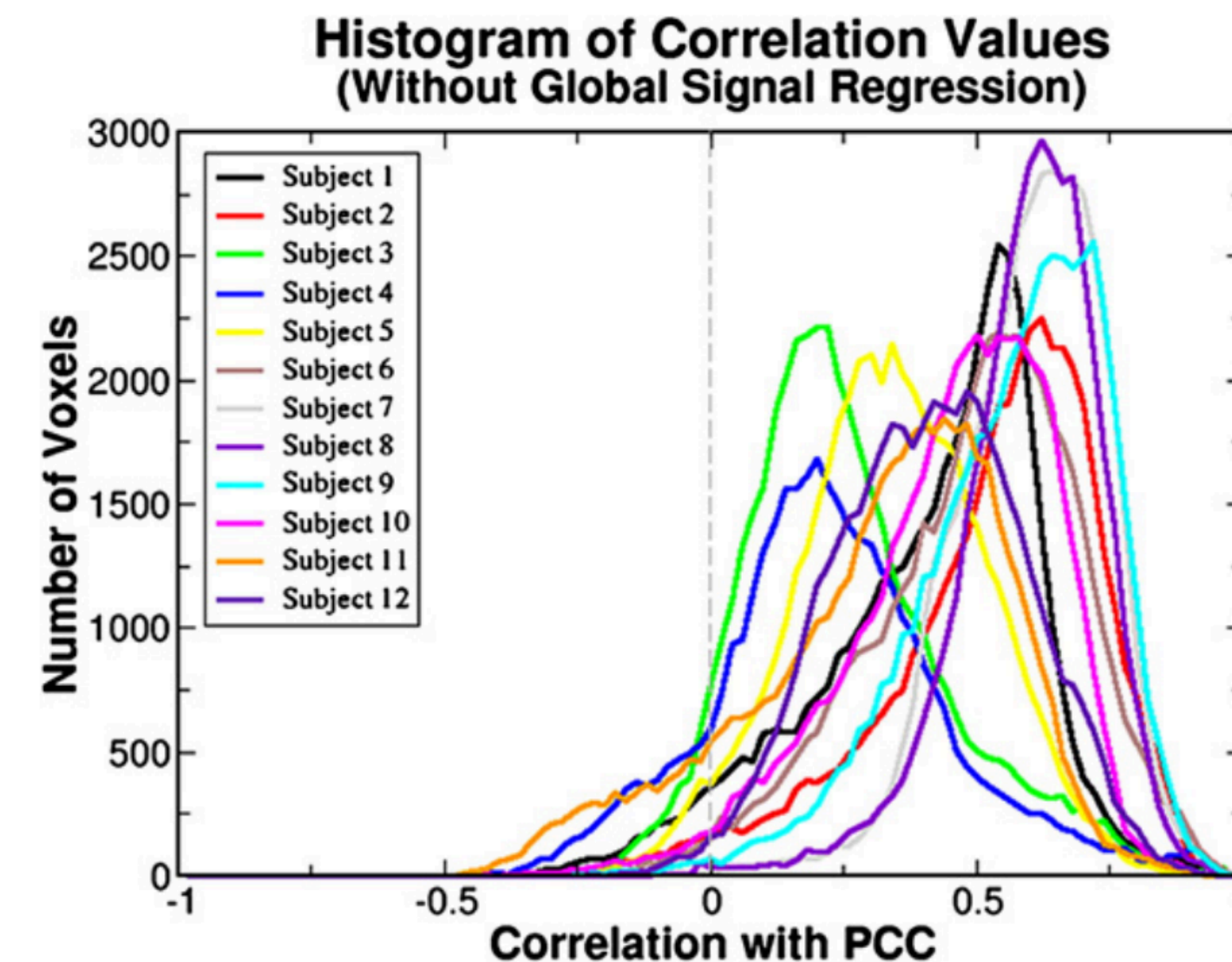


Global signal regression

去除全脑信号

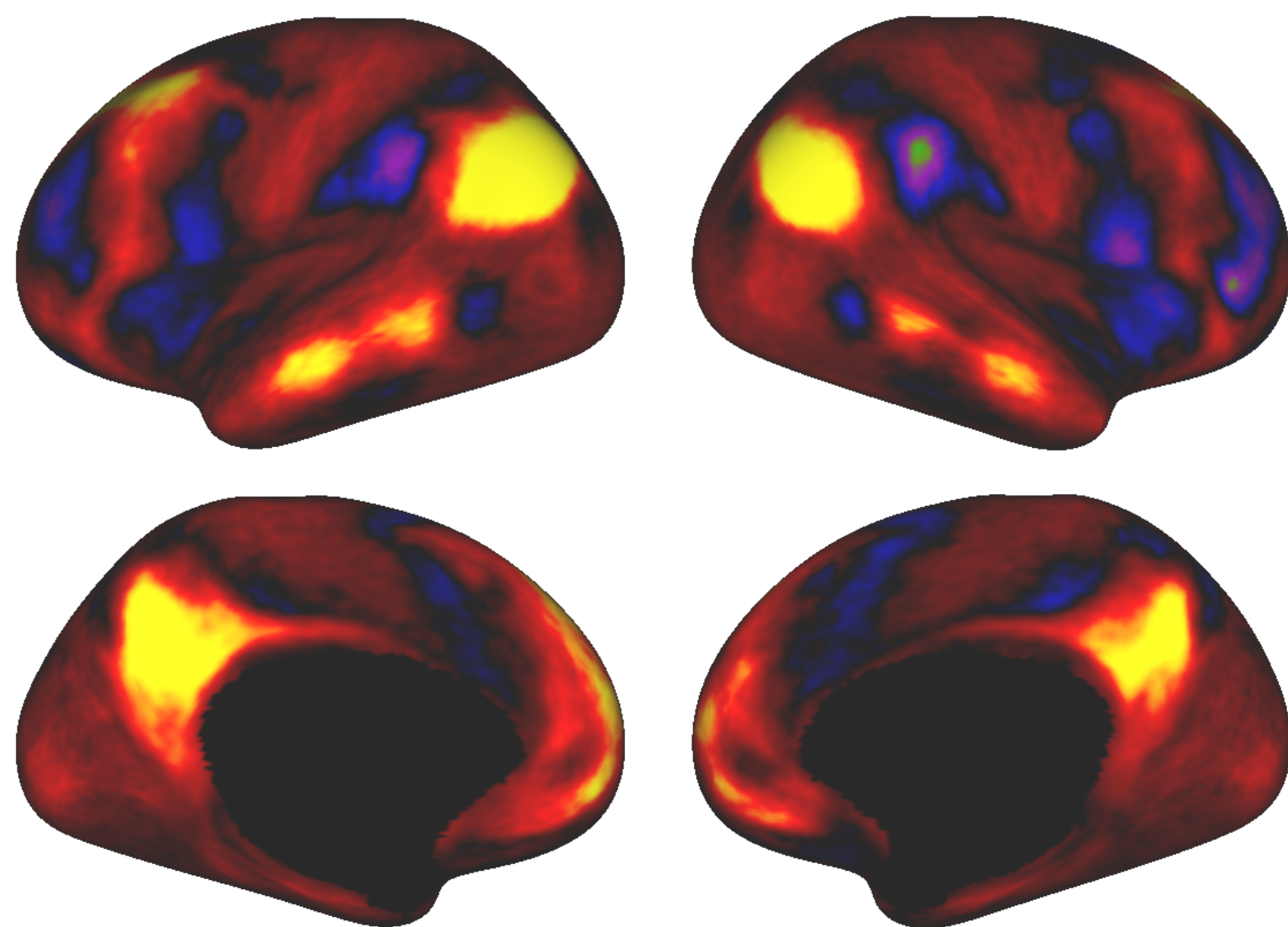
- Regress out mean timeseries across all voxels (or all grey matter voxels)
回归所有体素（或所有灰质体素）的平均时间序列
- Shifts connectivity values to be zero mean
将连通性值转换为零均值
- Therefore, more negative correlations
因此，存在更多的负相关
- Not necessary if using partial correlation
如果使用偏相关则不必要

Murphy et al (2009)



GSR effects & alternative

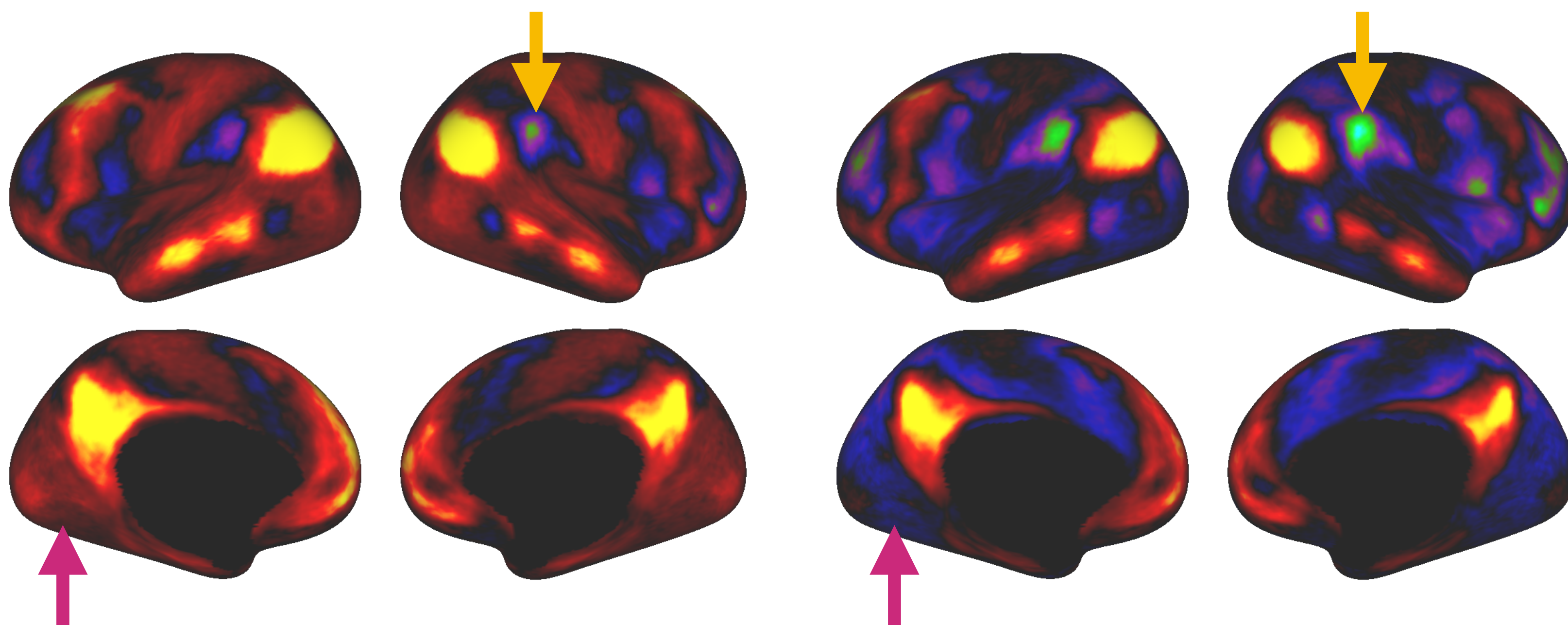
去除全脑信号效应和替代方法



PCC correlation
spatial ICA cleanup
PCC 相关
空间ICA去噪

GSR effects & alternative

去除全脑信号效应和替代方法

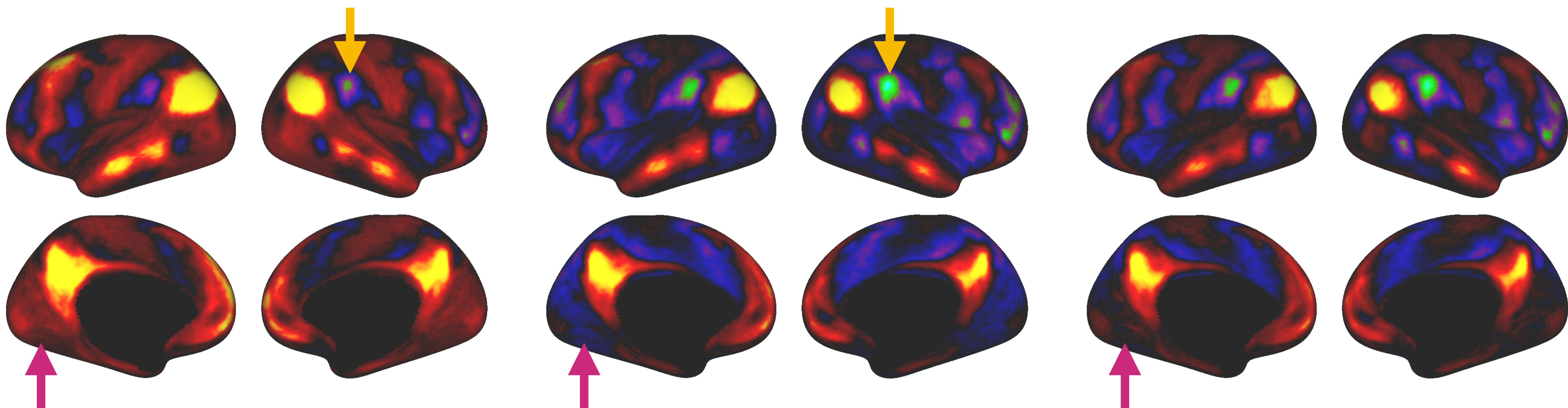


PCC correlation
 spatial ICA cleanup
 PCC 相关
 空间ICA去噪

PCC correlation
 spatial ICA cleanup + **GSR**
 PCC 相关
 空间ICA去噪 + **GSR**

GSR effects & alternative

去除全脑信号效应和替代方法



PCC correlation
 spatial ICA cleanup
 PCC 相关
 空间ICA去噪

PCC correlation
 spatial ICA cleanup + **GSR**
 PCC 相关
 空间ICA去噪 + **GSR**

PCC correlation
 spatial ICA cleanup + **temporal ICA cleanup**
 PCC 相关
 空间ICA去噪 + **时间ICA去噪**

Clean-up comparison

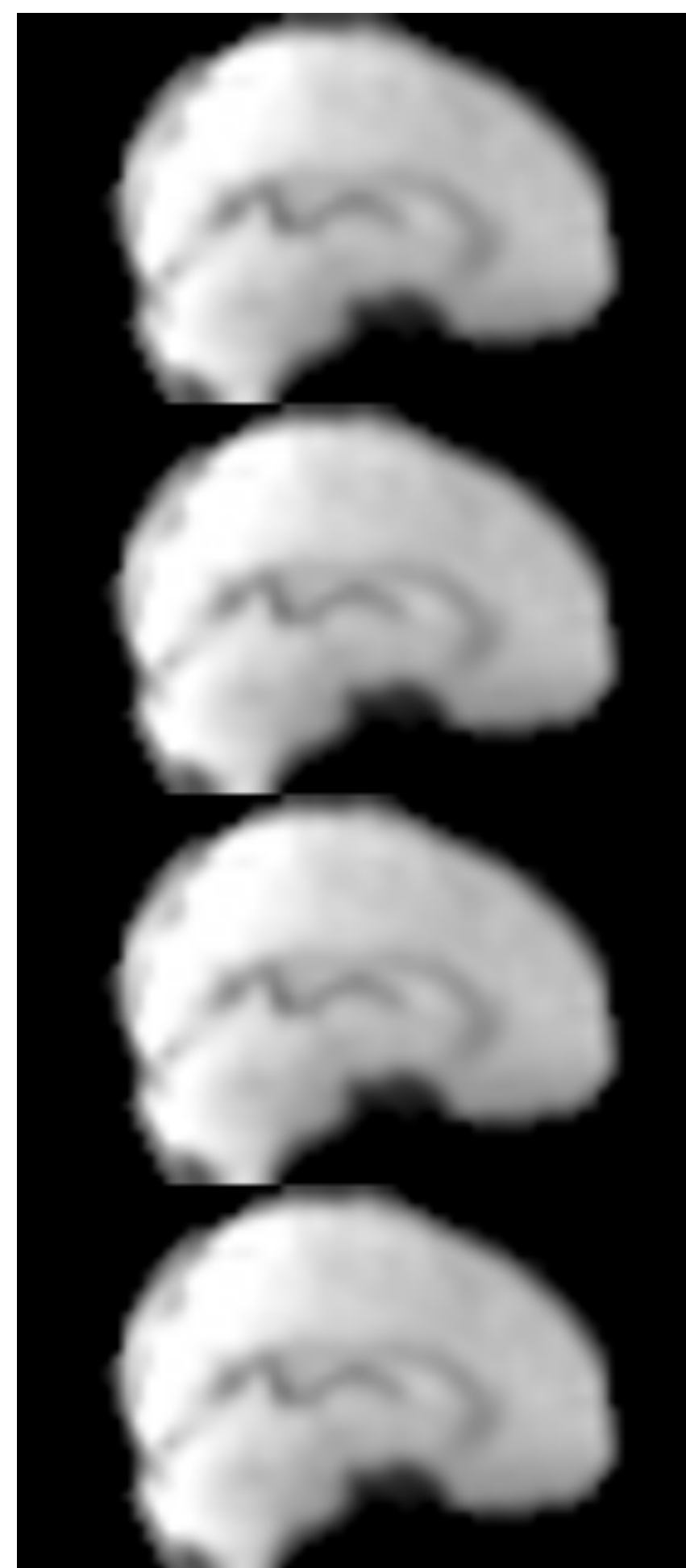
去噪比较

no additional correction
没有使用其他校正方法

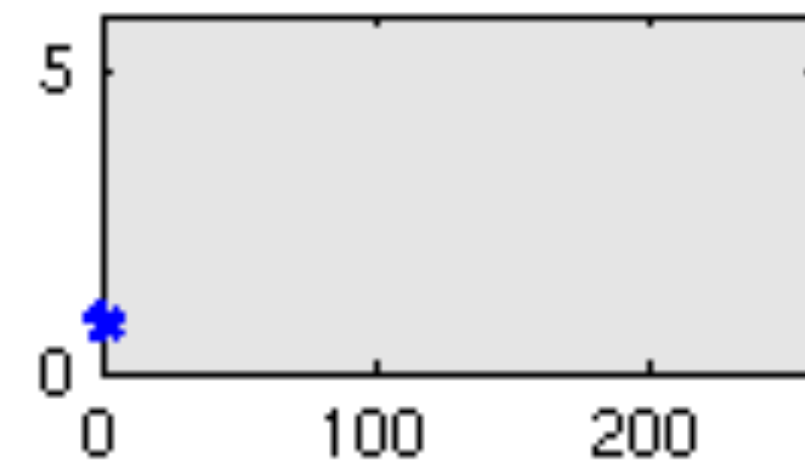
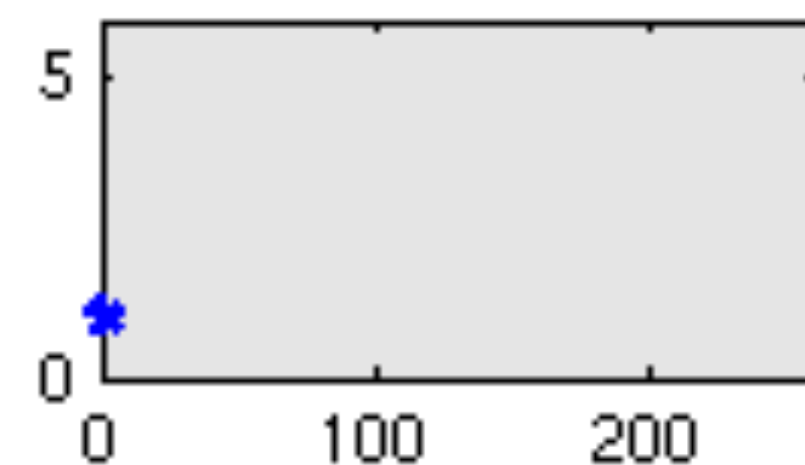
24RP-regression
24RP校正

24RP + volume censoring
24RP+体素检查

ICA-AROMA



FMRI data

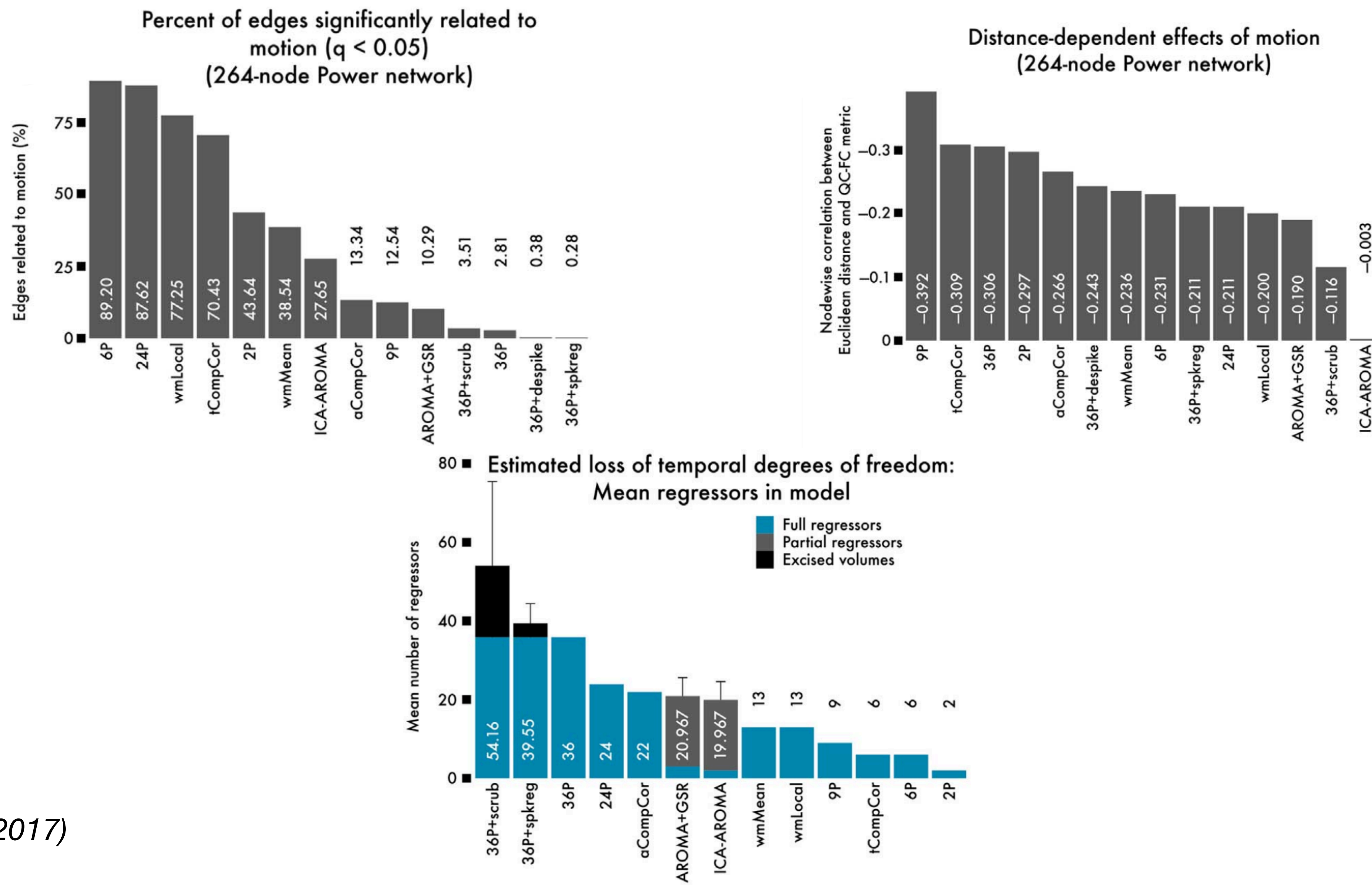


DVARS



Clean-up comparison

去噪比较





Preprocessing advice

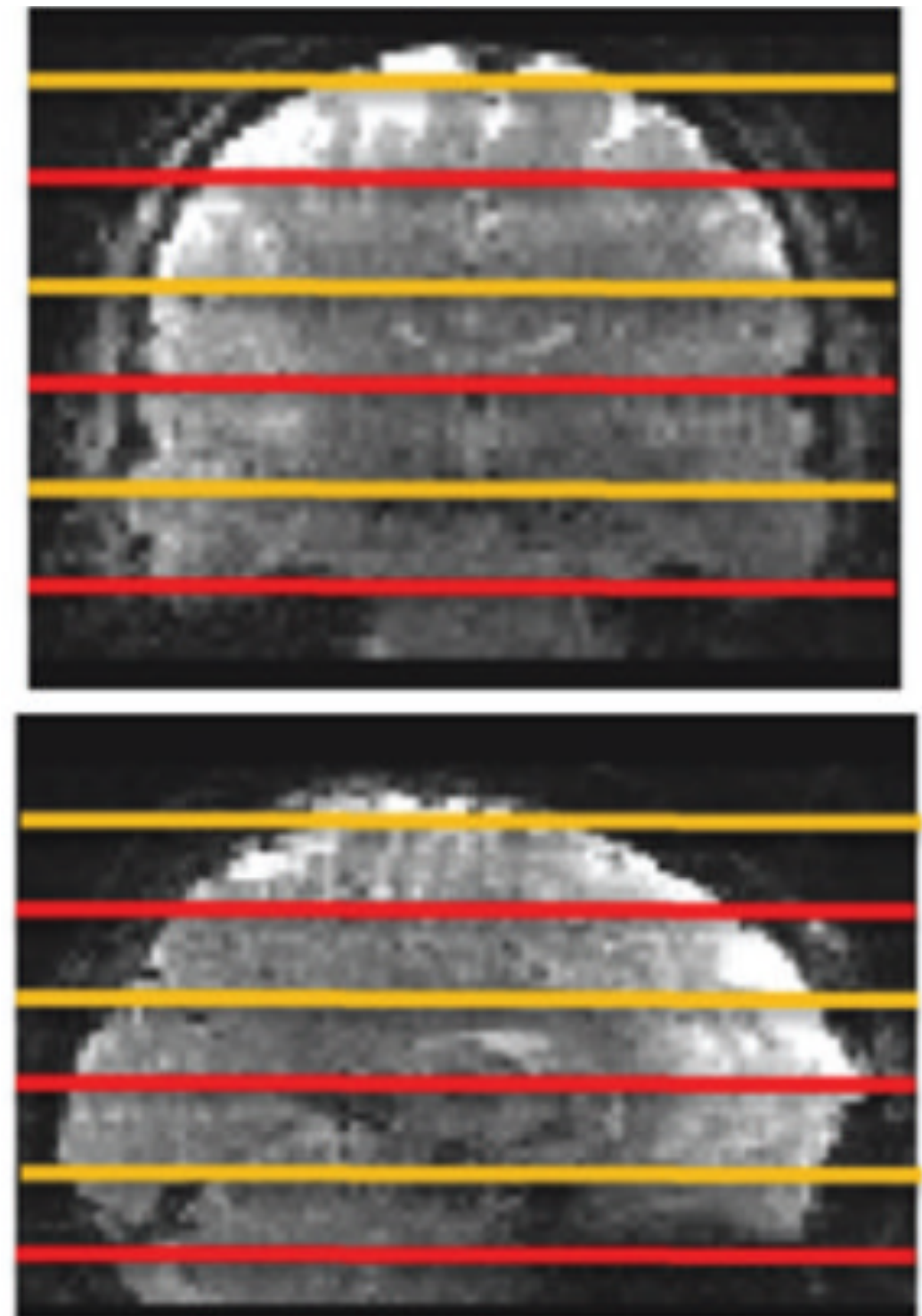
预处理建议

- Read up on the latest literature 阅读最新文献
- Nuisance regression is not enough 噪声回归是不够的
- Low-pass filtering is not enough & often not necessary when using other approaches 低通滤波是不够的，在使用其他方法时通常不需要
- Use ICA-based methods and/or volume censoring
使用基于ICA的方法和/或全脑检查
- Use physiological noise regression when interested in brainstem or other vulnerable brain regions 当对脑干或其他敏感的大脑区域感兴趣时，使用生理噪声回归
- Don't use global signal regression 不要回归全脑信号

Data acquisition advice

数据采集建议

- Just a guide, may vary depending on study aims!
只是一个建议，可能会根据研究目标而有所不同!
- Whole brain coverage, voxelsize: 2 - 3 mm
全脑覆盖，体素大小：2-3毫米
- Scan duration: 扫描持续时间
 - 10-15 minutes per scan 每次扫描10-15分钟
 - Potentially multiple scans 可以多次扫描
- Repetition time: ideally close to 1 second (multiband/
multiplexed imaging) 重复时间：理想情况下接近1秒（多频段/多路复用成像）
- Paradigm: eyes open, fixation cross 范式：睁眼，固定十字架
- Auxiliary data: physiology, sleep 辅助数据：生理，睡眠





Network modelling analysis

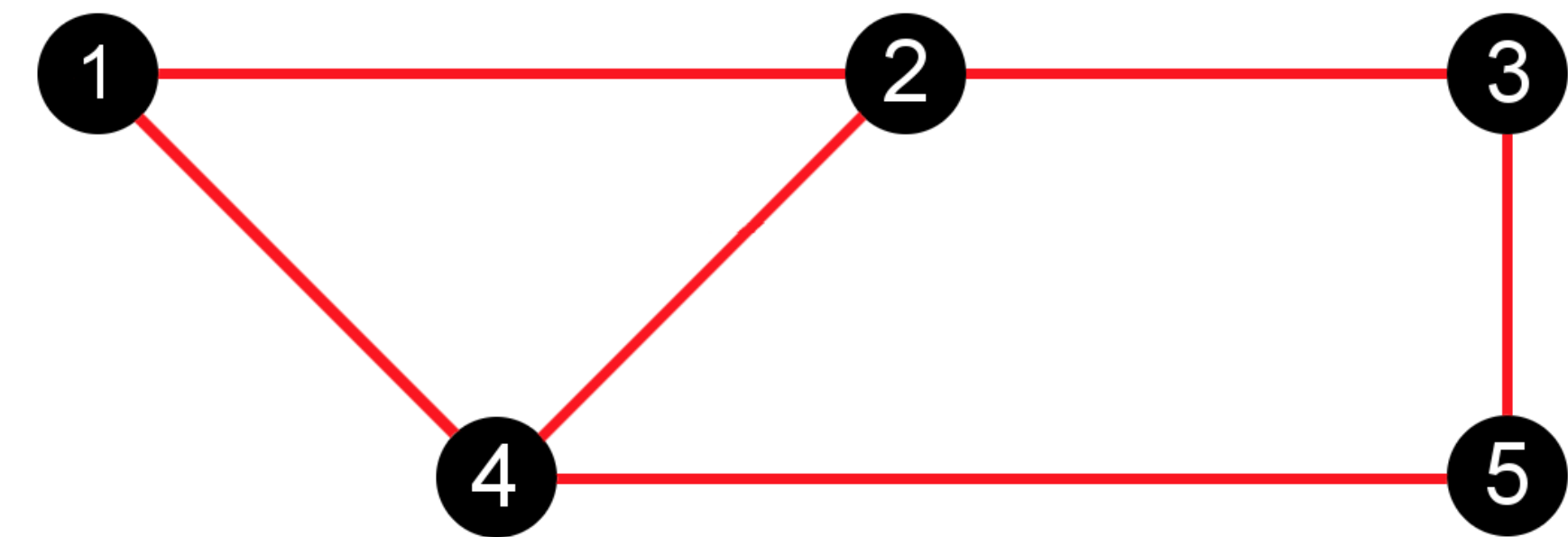
网络建模分析



Glossary

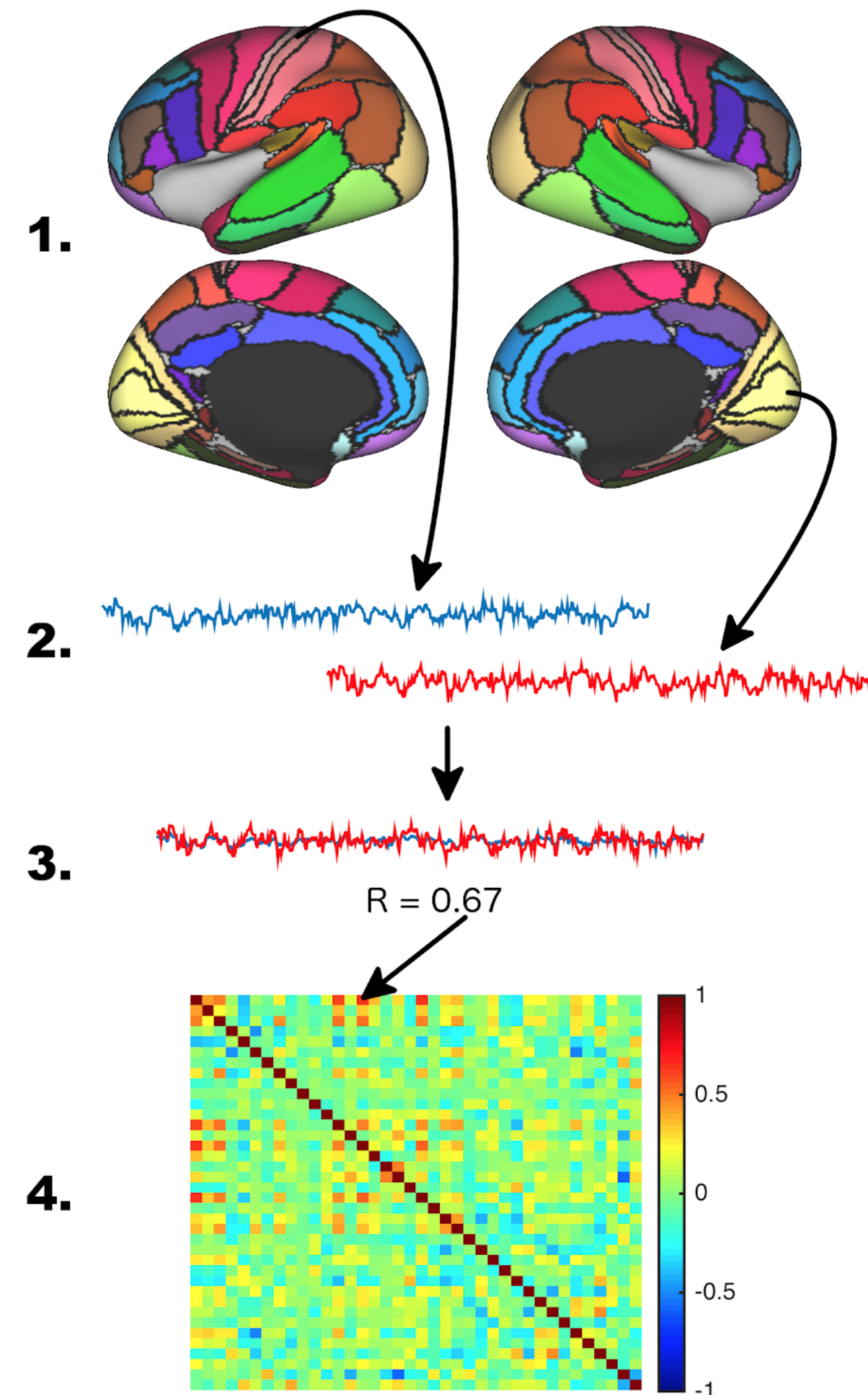
词汇表

- Node = functional brain region 节点=功能性大脑区域
 - Contiguous nodes = interconnected 'blobs' 连续节点=互连'节点'
 - Non-contiguous nodes = e.g. bilateral 非连续节点=例如双边
- Parcellation = separation of all voxels into a set of nodes
- 分区 = 将所有体素分离为一组节点
 - Hard parcellation = binary regions 二进制区域
 - Soft parcellation = weighted regions 加权区域
- Edge = connection between nodes 边缘=节点之间的连接
- Connectomics = mapping all connections between all brain regions
连接组 = 映射所有大脑区域之间的所有连接



Analysis steps

分析步骤



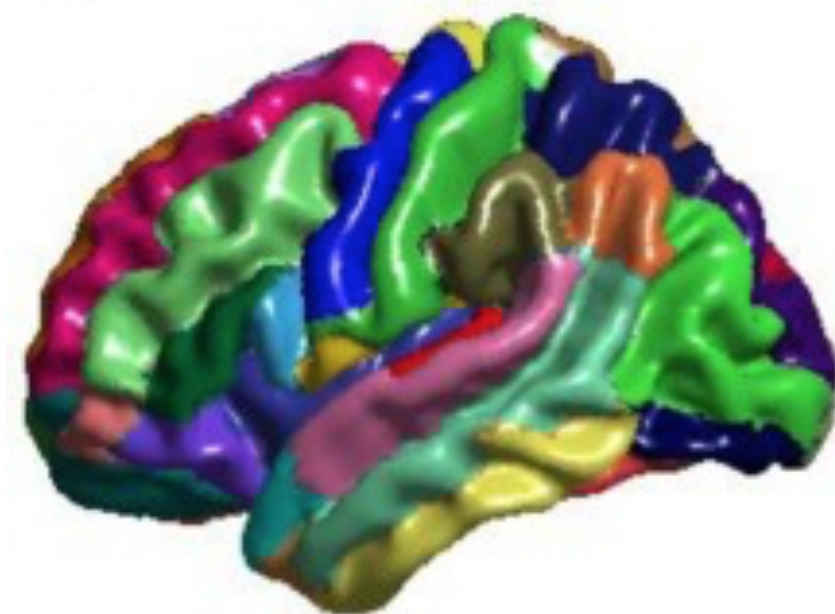
- Node definition 节点定义
- Timeseries extraction 时间序列提取
- Edge calculation 边缘计算
- Network matrix 网络矩阵
- Group analysis 组分析

Node definition

节点定义

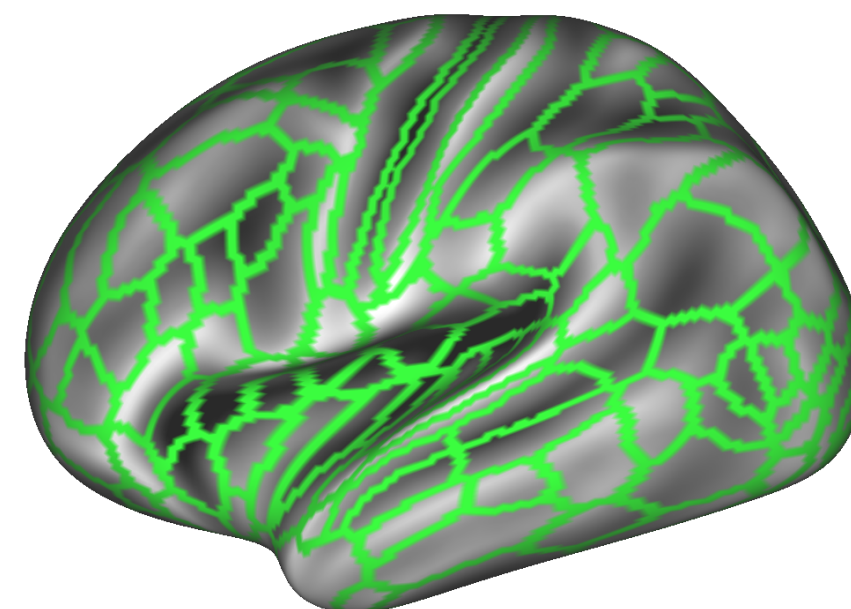
Anatomical atlases

结构模板



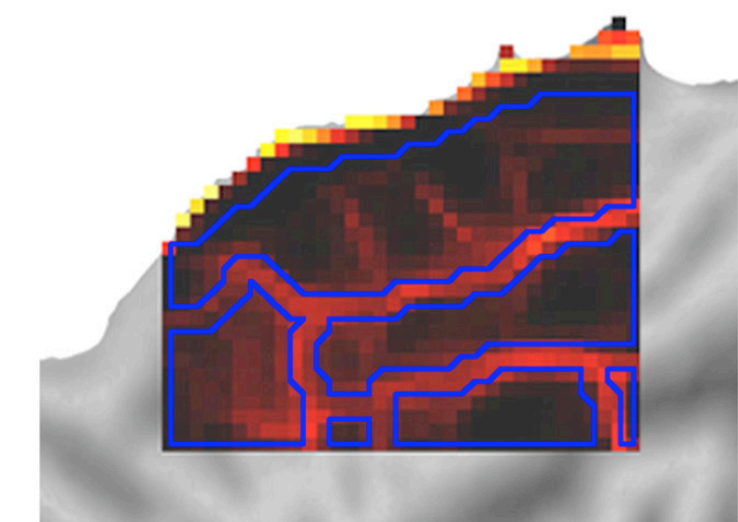
Functional atlases

功能模板



Data-driven parcellation

数据驱动分区

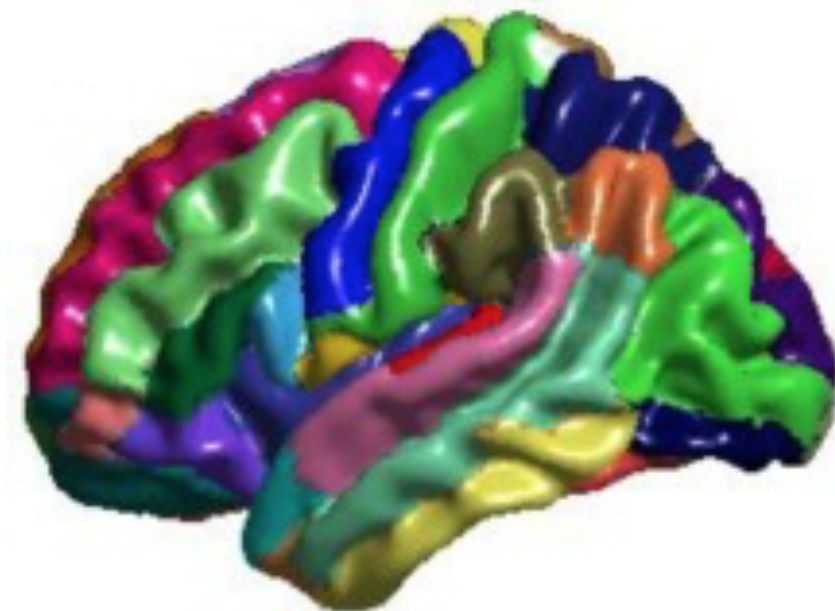


Node definition

节点定义

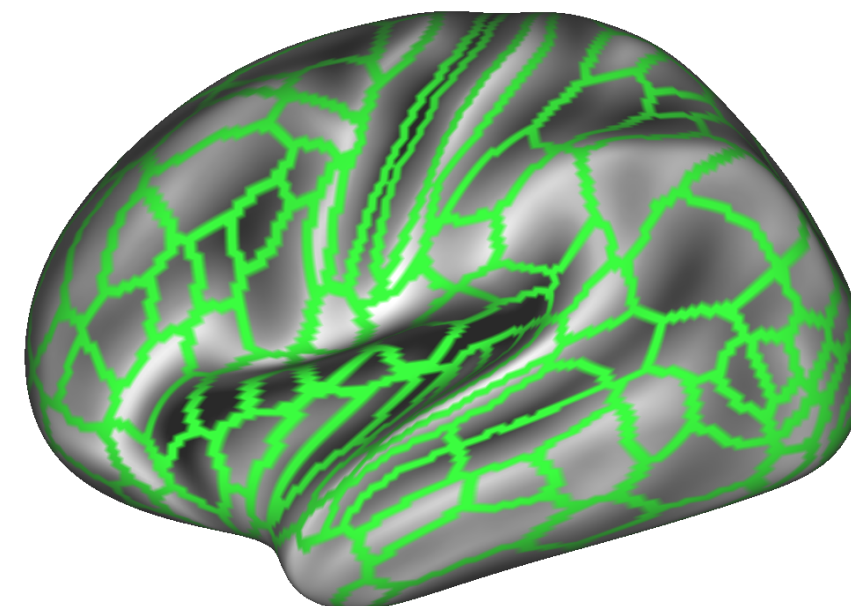
Anatomical atlases

- Harvard-Oxford/ AAL
哈佛/AAL
- Avoid if possible because typically based on small number of subjects and not a good estimation of functional boundaries

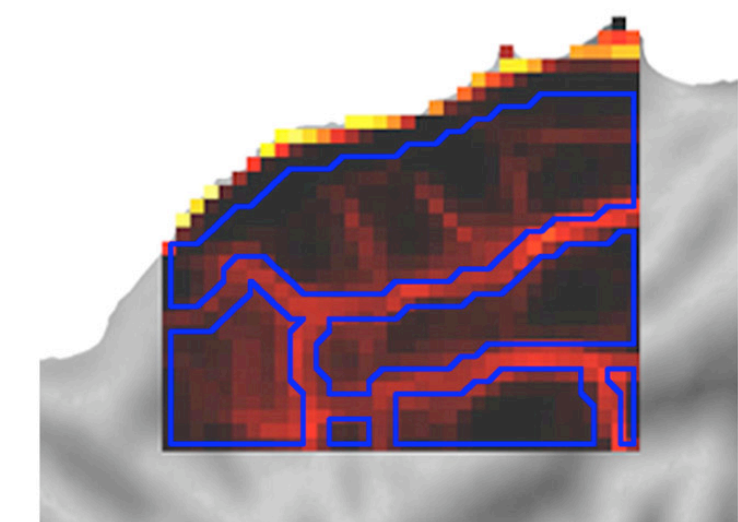


Functional atlases

尽可能避免，因为通常基于少量被试，对功能边界不能良好的估计



Data-driven parcellation

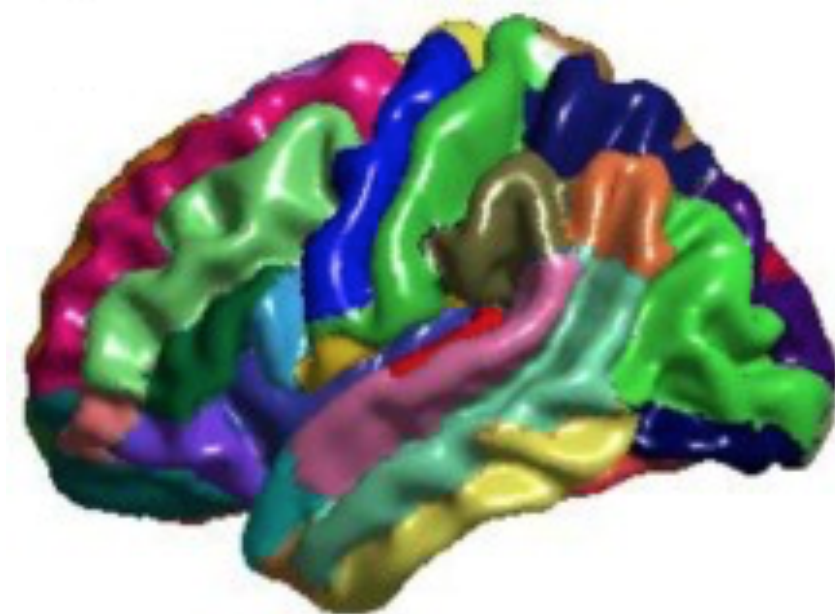


Node definition

节点定义

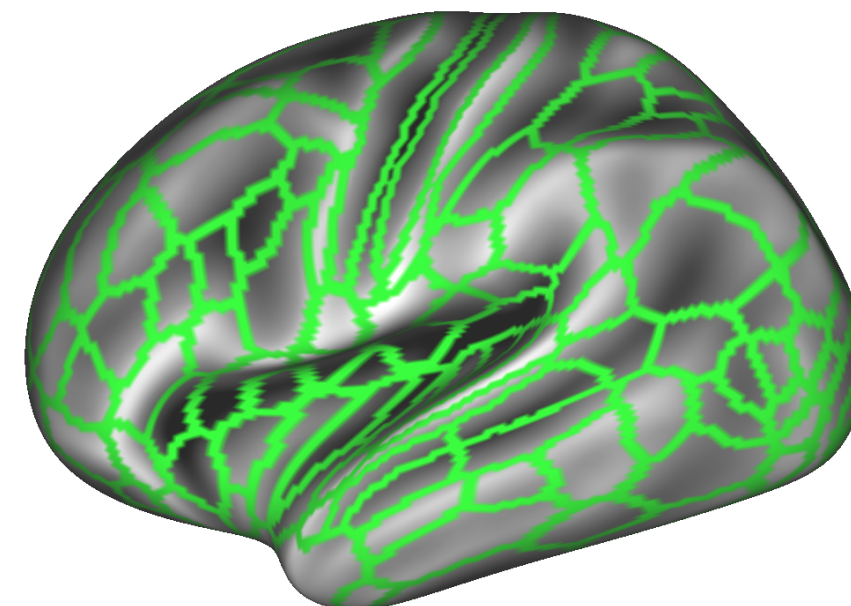
Anatomical atlases

- Harvard-Oxford/ AAL
- Avoid if possible because typically based on small number of subjects and not a good estimation of functional boundaries



Functional atlases

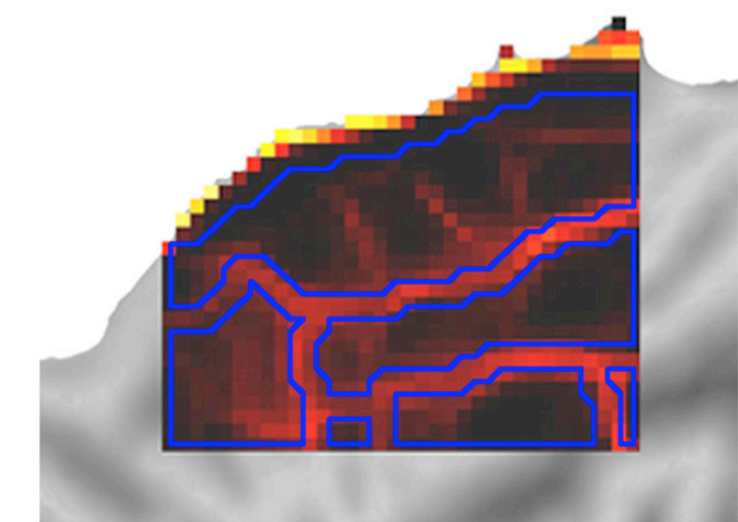
- Yeo 2011/ Glasser 2016
- Many good functional atlases available, though few comparison studies
- How to map onto individuals is very important



Data-driven parcellation

虽然很少有比较研究，但可以使用许多功能良好的模板

如何映射到个体空间是非常重要的

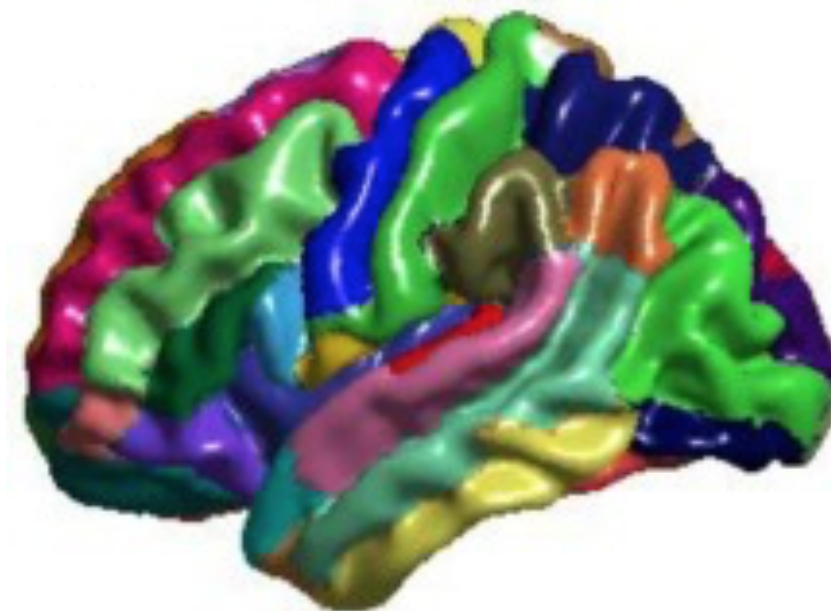


Node definition

节点定义

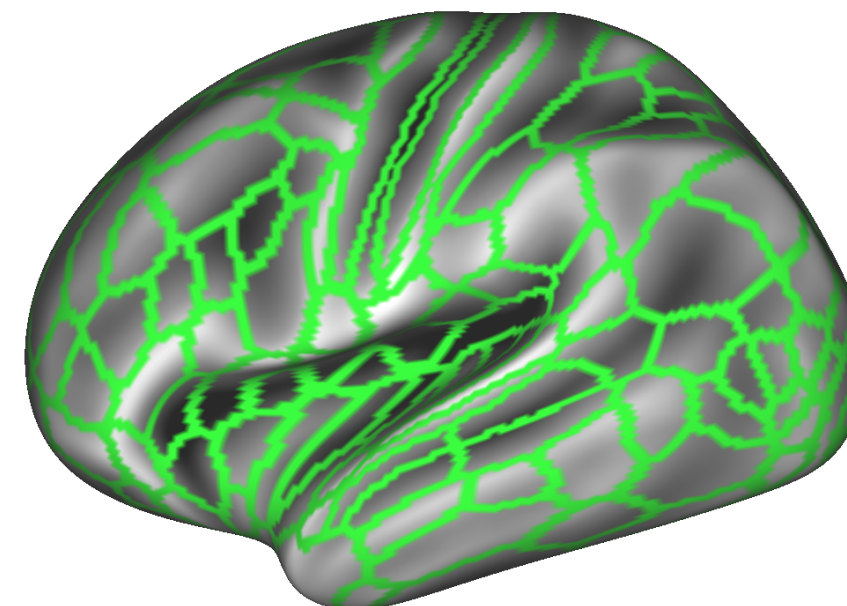
Anatomical atlases

- Harvard-Oxford/ AAL
- Avoid if possible because typically based on small number of subjects and not a good estimation of functional boundaries



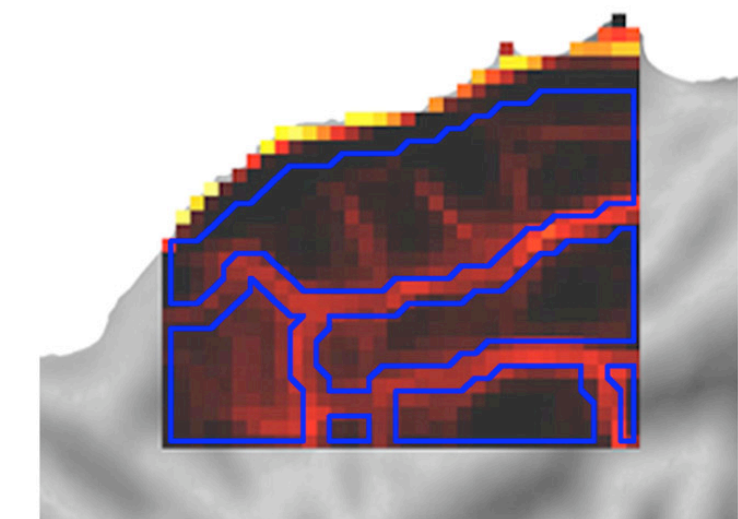
Functional atlases

- Yeo 2011/ Glasser 2016
- Many good functional atlases available, though few comparison studies
- How to map onto individuals is very important



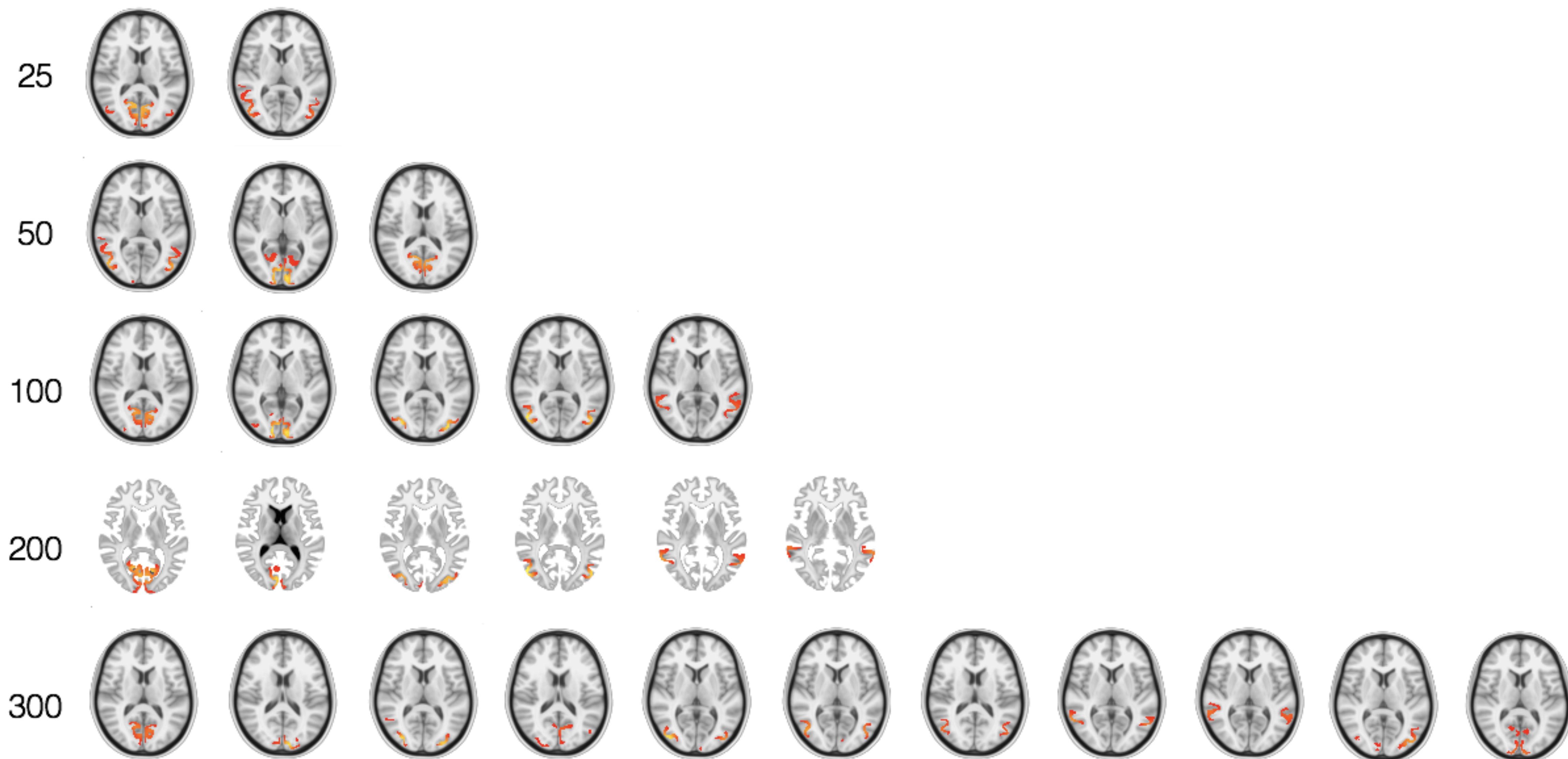
Data-driven parcellation

- ICA/ Clustering/ Gradients
- Estimate parcellation from the same dataset used for further analyses
从用于进一步分析的相同数据集中估算分区
- How to map group parcellation onto individuals very important
如何将组分割映射到个体非常重要



ICA for parcellation

ICA分区



Timeseries extraction

时间序列提取

Hard parcellation:

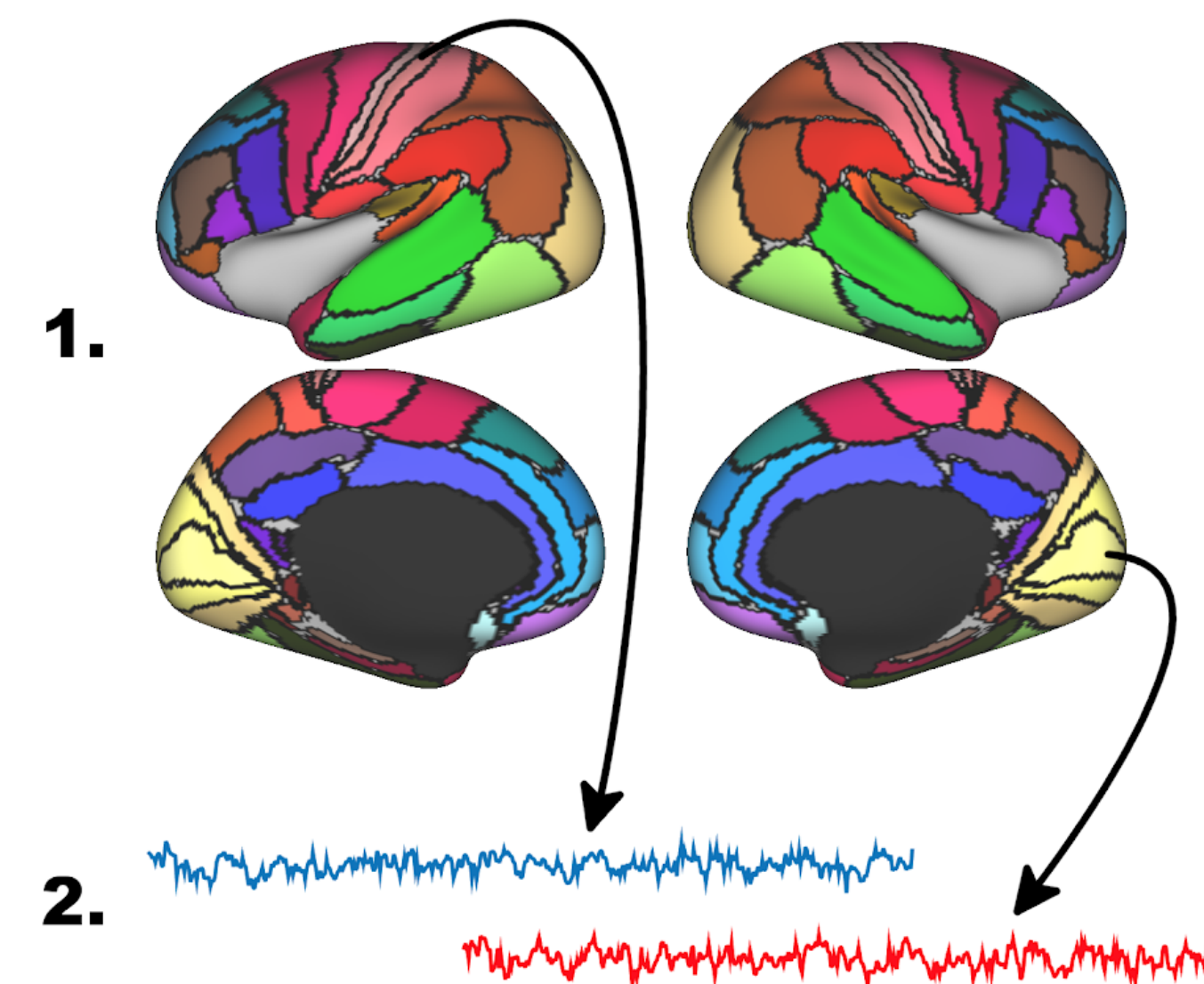
- Masking (mean timeseries) 掩板 (平均时间序列)
- Eigen timeseries (PCA) 特征时间序列 (PCA)
- Using multilayer classifier 使用多层分类器

ICA (soft parcellation):

- **Thresholded** dual regression/ back projection
阈值双重回归/反投影

Alternative: 其他

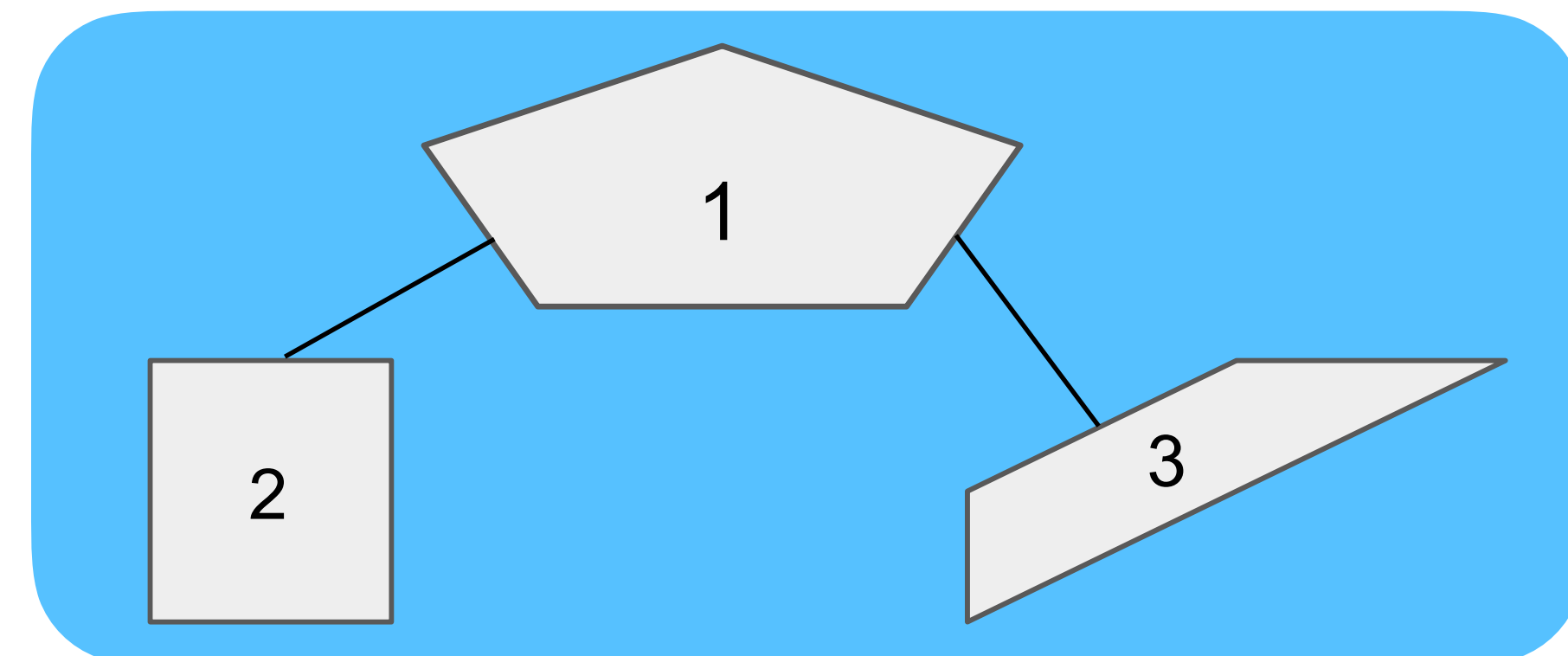
- Hierarchical estimation of group & subject 组、个体的分层估计
- e.g. PROFUMO



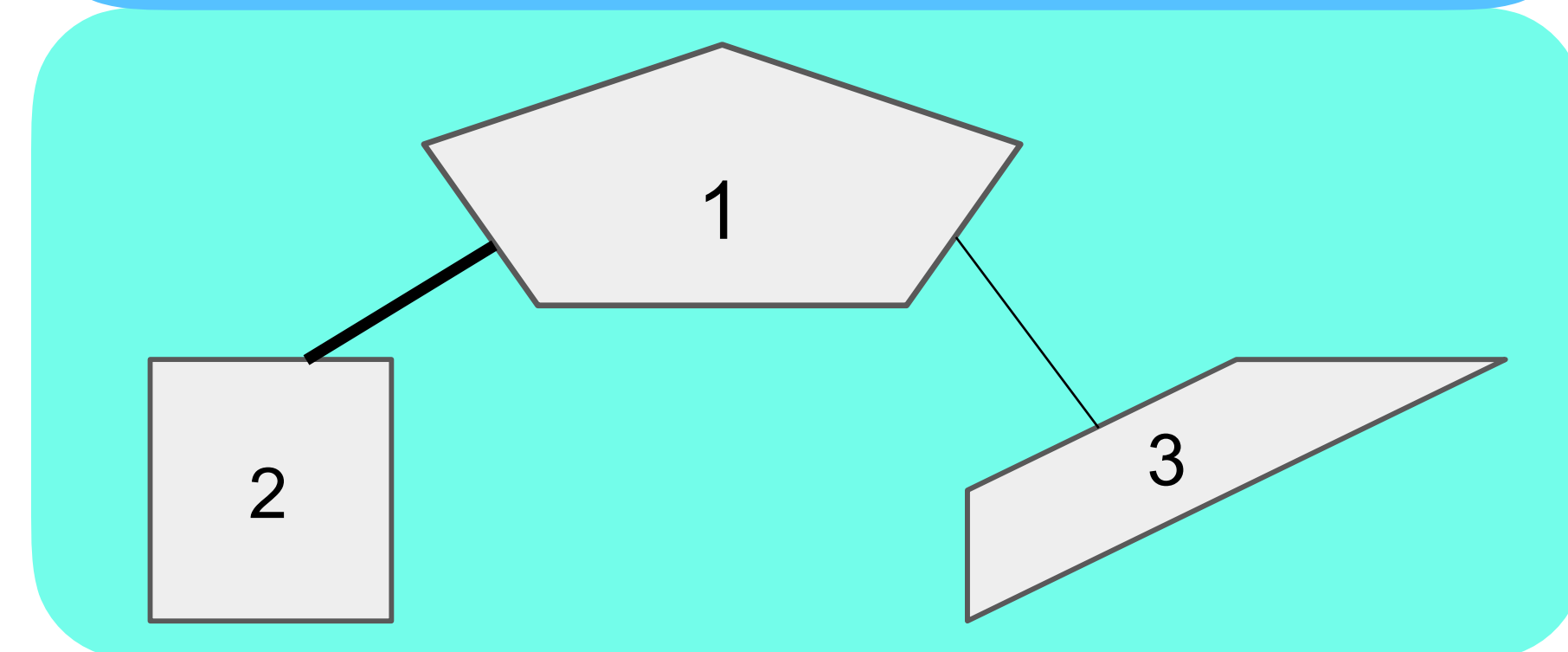
Edge calculation

边缘计算

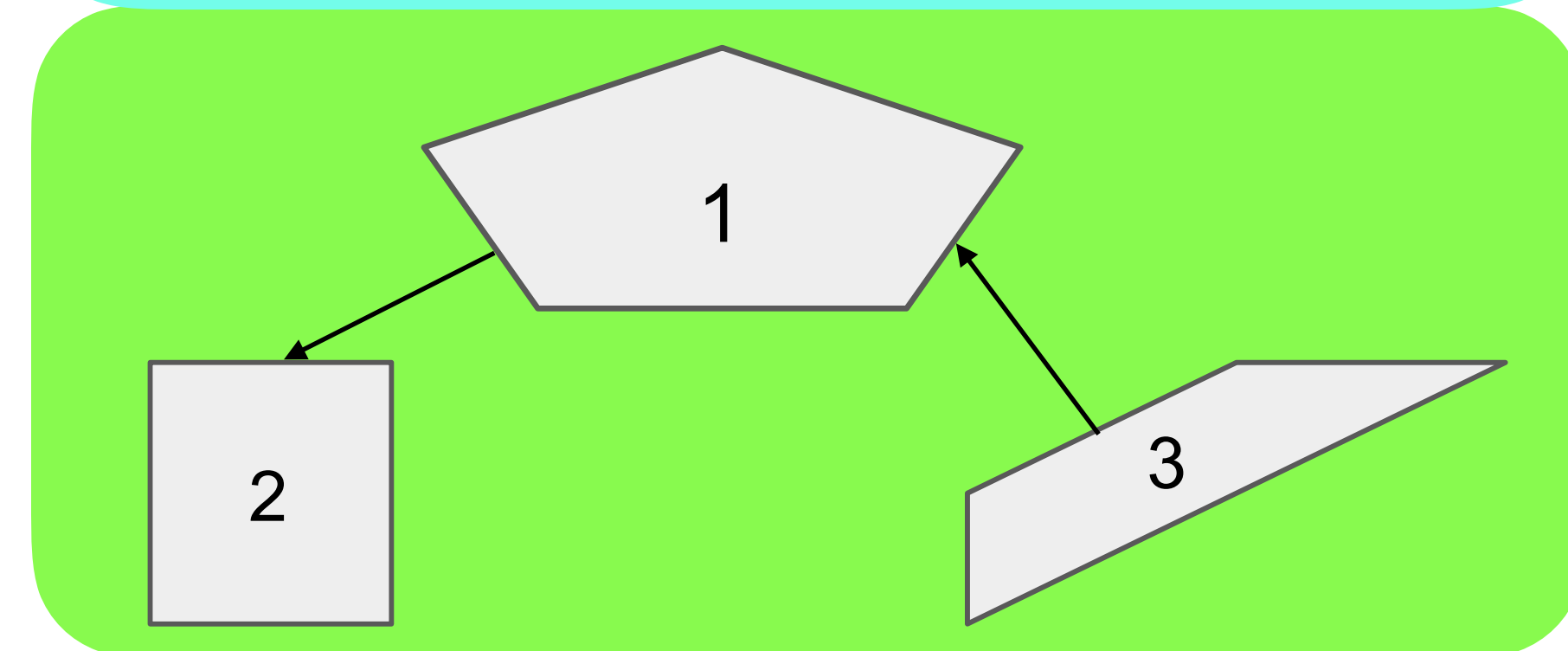
- Presence/ absence of edges 存在/不存在边缘



- Strength of edges 边缘强度



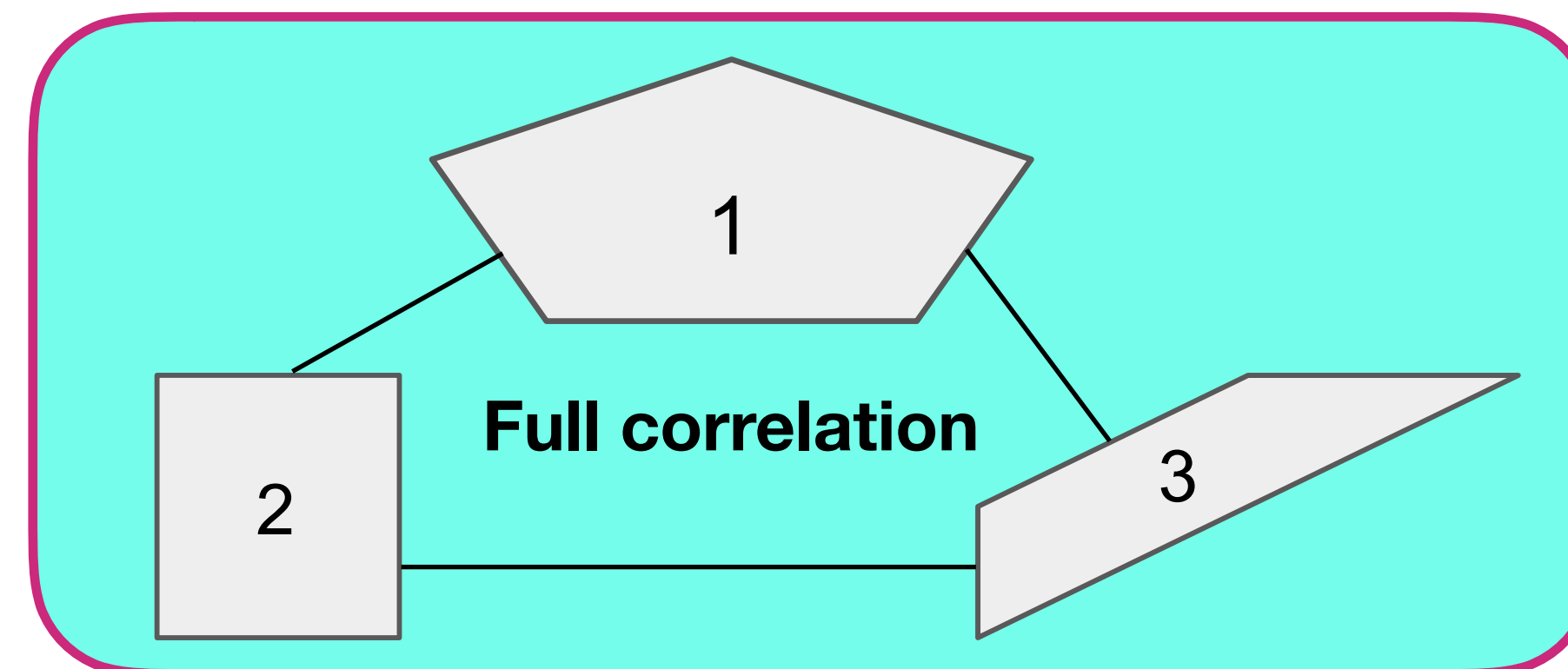
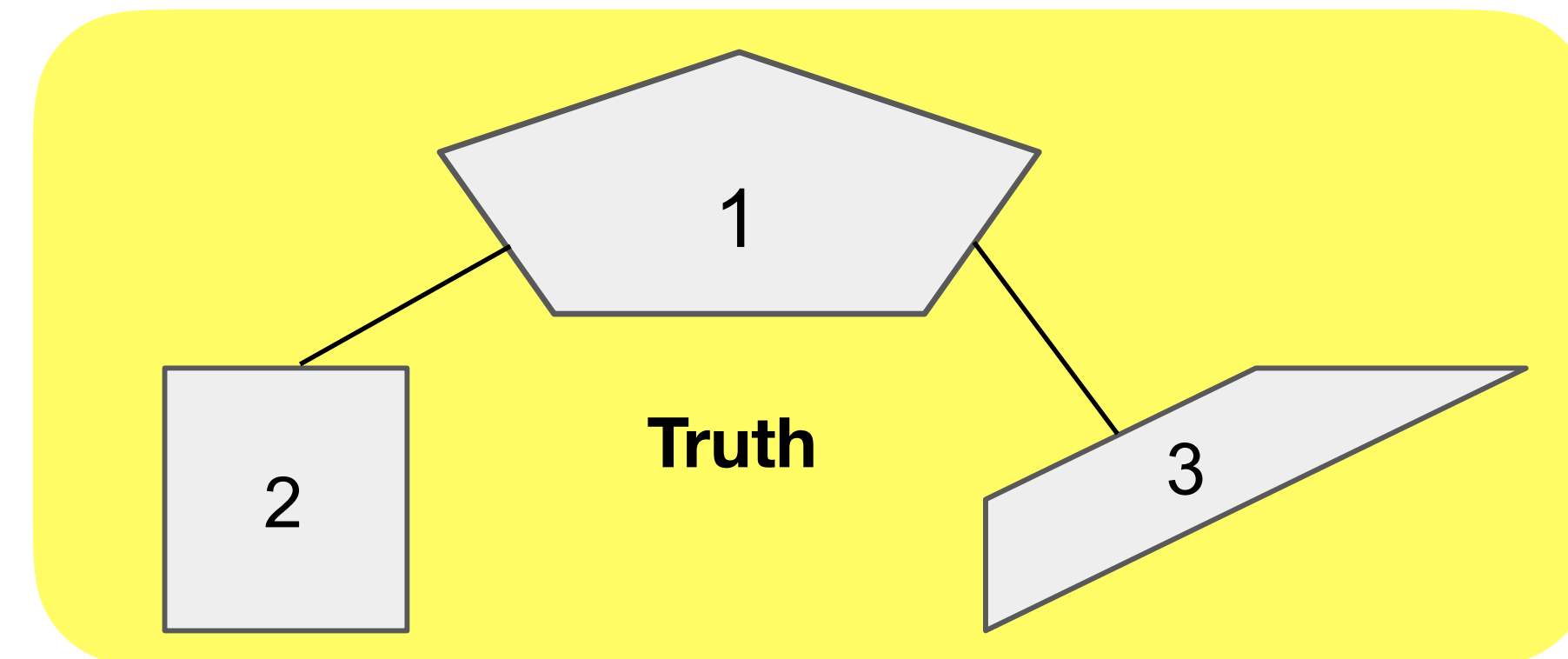
- Directionality of edges 边缘的方向性



Direct versus indirect connections

直接连接与间接连接

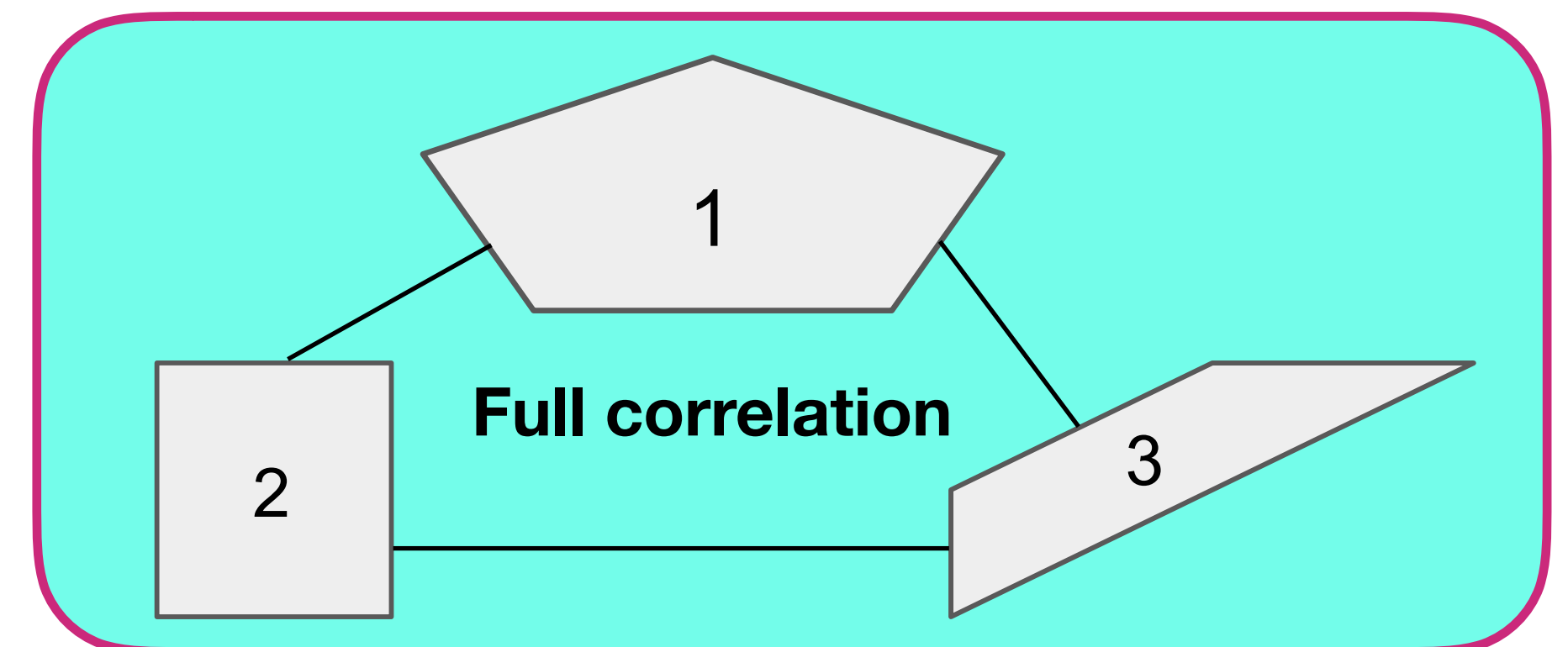
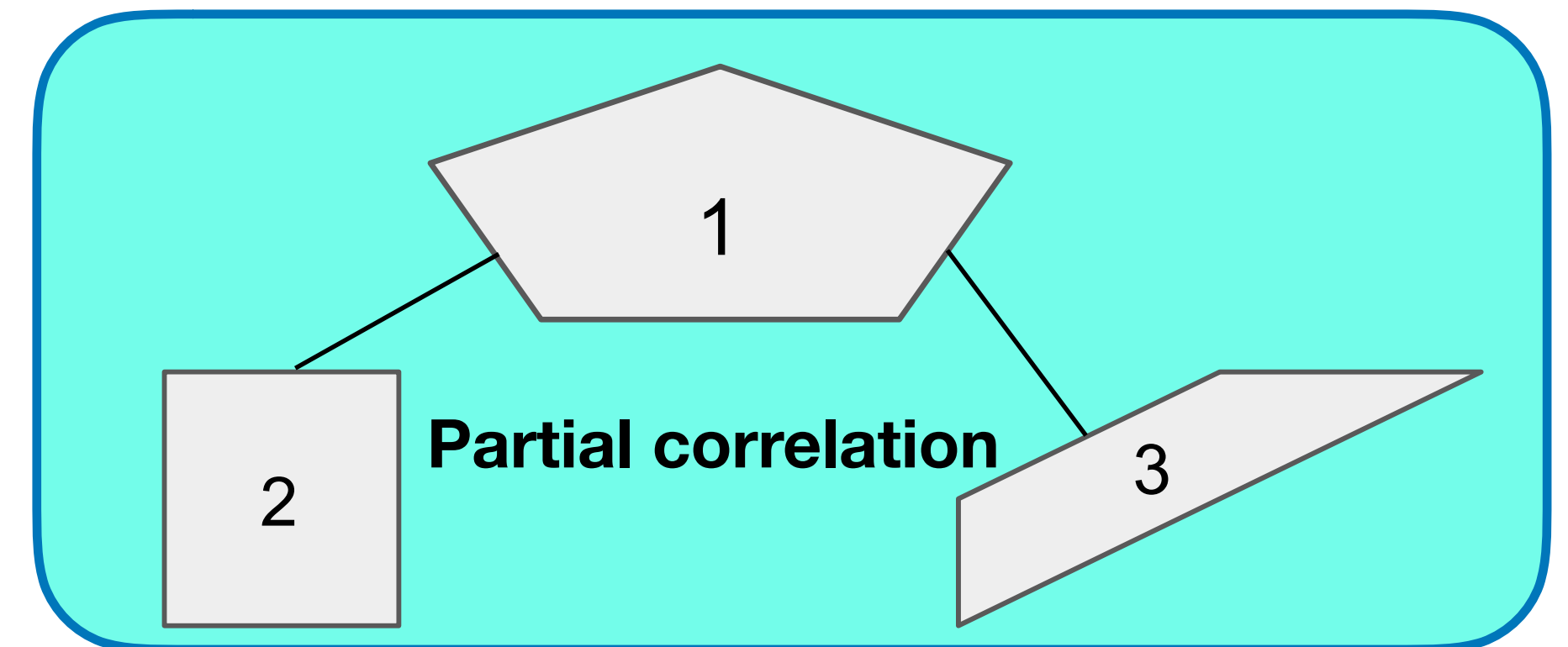
- Correlation between 2 and 3 will exist
2和3之间存在相关性
- Therefore full correlation will
incorrectly estimate connection 2-3
因此，完全相关将错误地估计连接2-3
- 2-3 is an indirect connection
2-3是间接连接



Partial correlation

偏相关

- Before correlating 2 and 3, first regress 1 out of both (“orthogonalise wrt 1”) 在关联2和3之前，首先从两者中回归1 (“正交wrt 1”)
 - If 2 and 3 are still correlated, a direct connection exists 如果2和3仍然相关，则存在直接连接
- More generally, first regress all other nodes’ timecourses out of the pair in question 更一般地说，首先从所讨论的对组中回归所有其他节点的时间序列
 - Equivalent to the inverse covariance matrix 等效于逆协方差矩阵





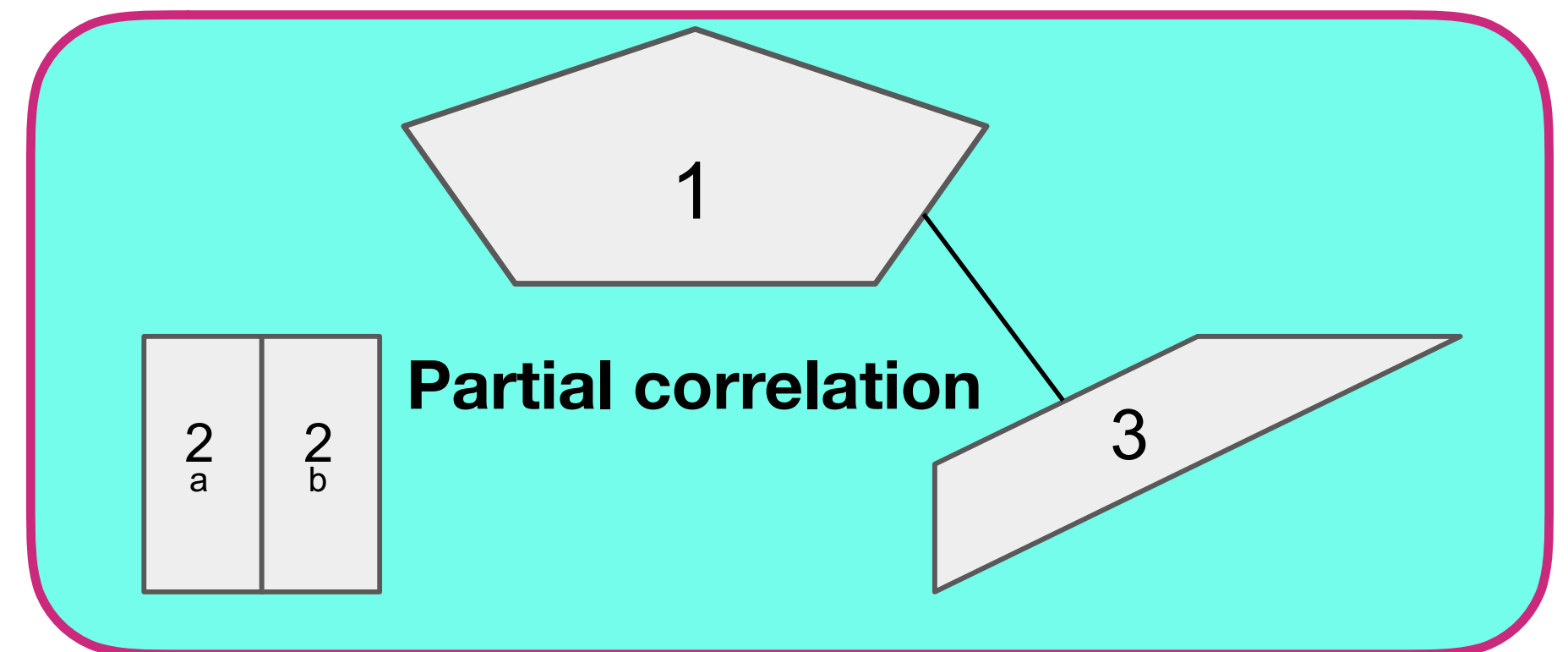
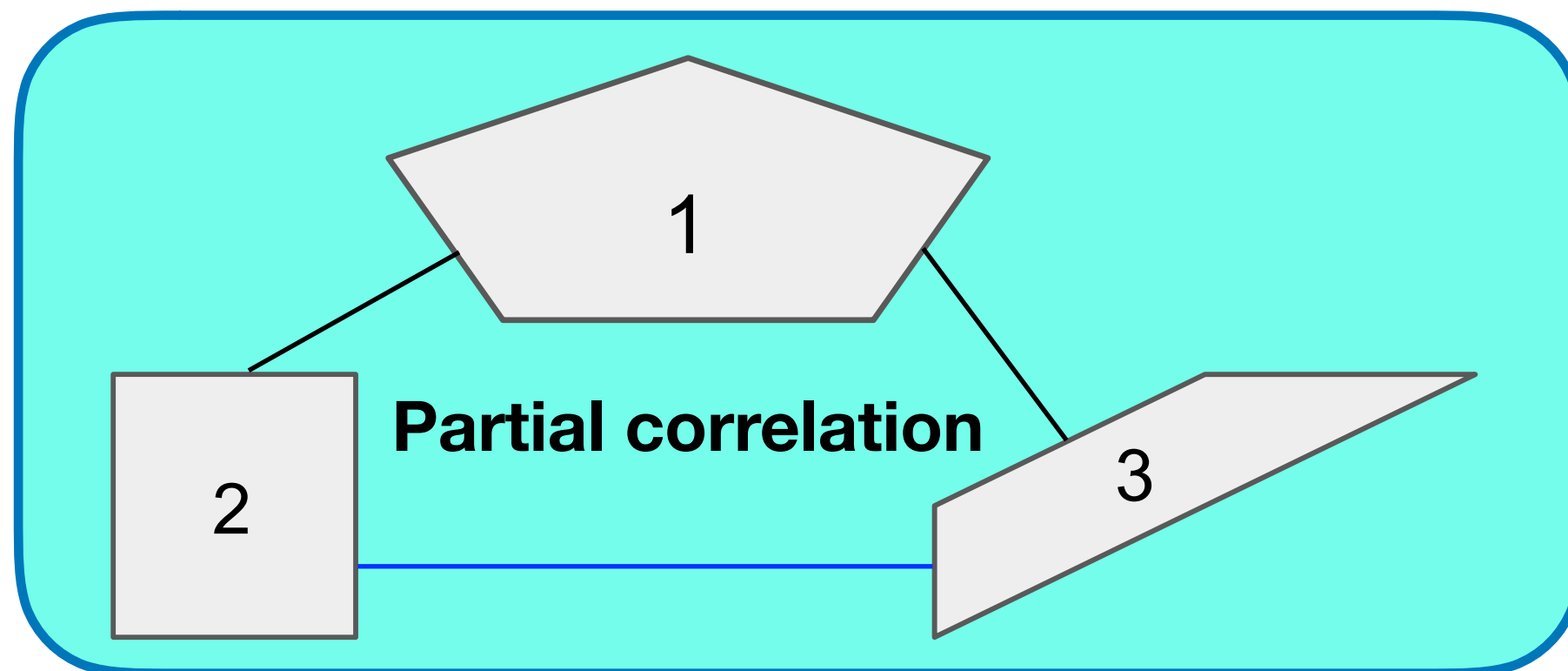
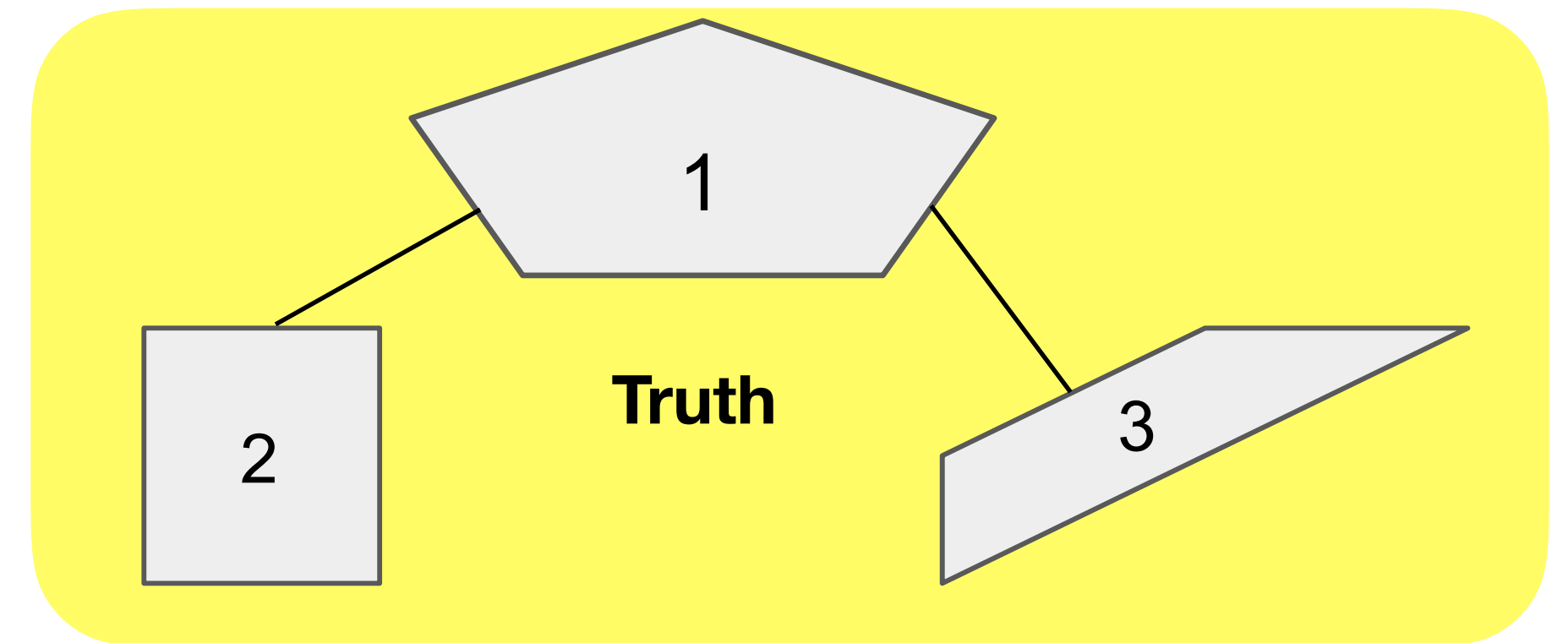
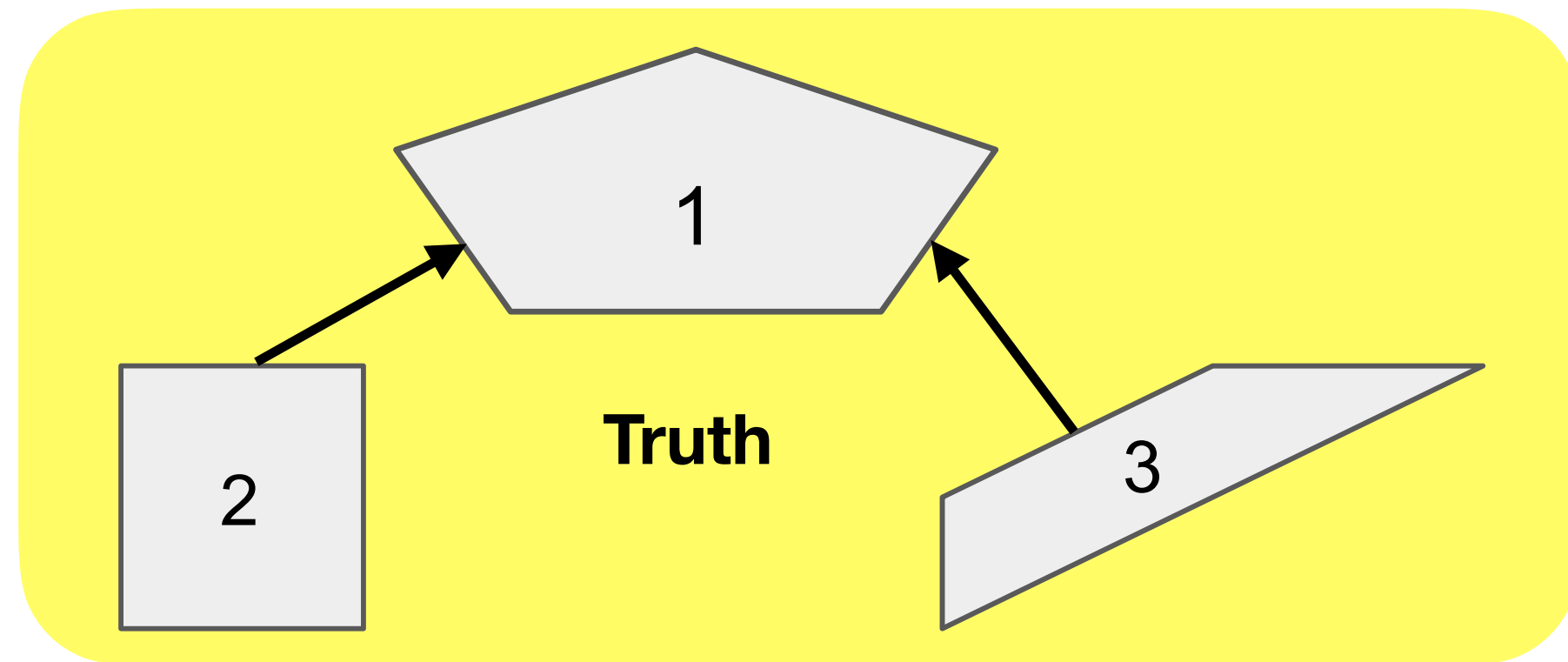
Regularisation

正规化

- Urgh! If you have 200 nodes and 100 timepoints, this is impossible!Urgh!
如果你有200个节点和100个时间点，这是不可能的!
- A problem of DoF - need large #timepoints - #nodes DoF的问题 - 需要大的#时间点 - #节点
- When inverting a “rank-deficient” matrix it is common to aid this with some mathematical conditioning, e.g. force it to be sparse (force low values that are poorly estimated to zero)
当反转“秩不足”矩阵时，通常用一些数学条件来辅助它，例如，强制它稀疏（强制估计为零的低值）
- Regularised partial correlation (such as ICOV, Ridge) 正则化的偏相关（如ICOV, Ridge）
- But still important to maximise temporal degrees of freedom 但是最大化时间自由度仍然很重要

Need to carefully define nodes

需要仔细定义节点



Berkson's paradox = false positive (2-3)

伯克森悖论=误报 (2-3)

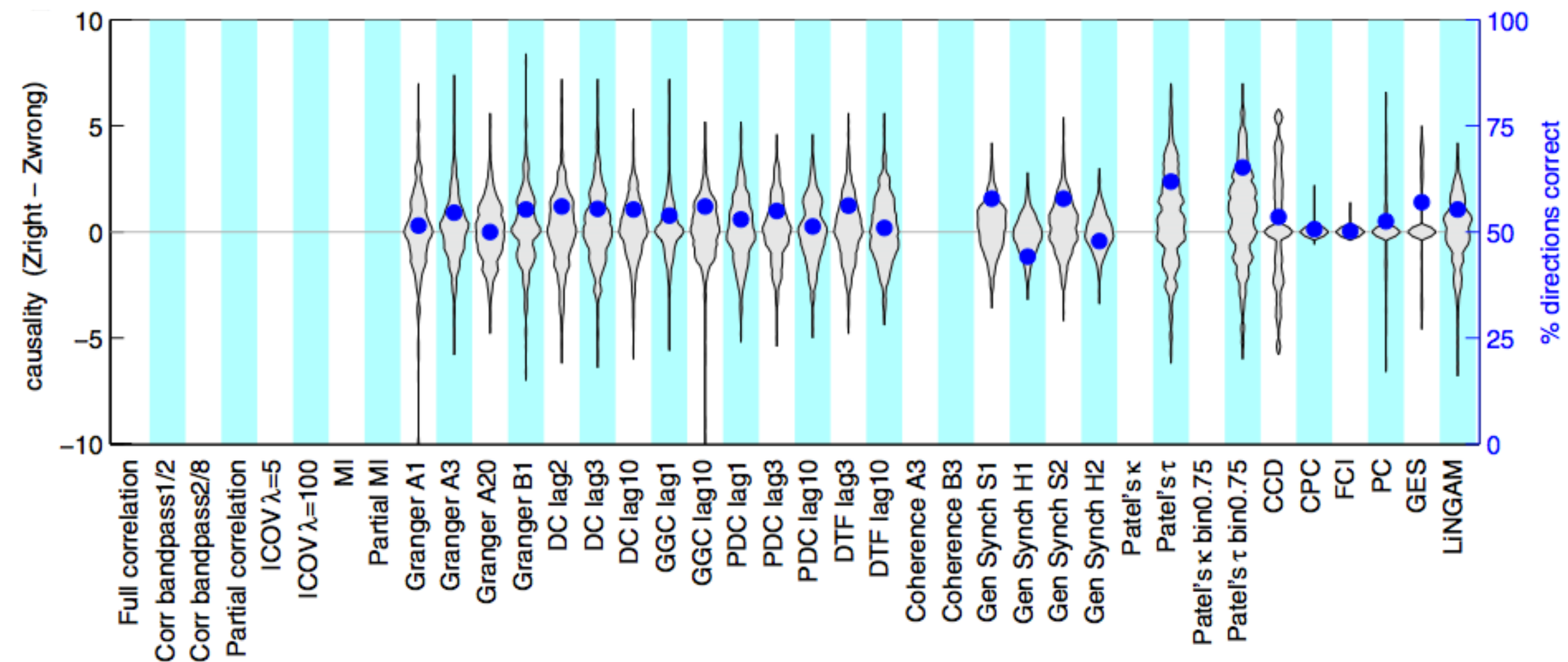
Over-splitting = false negative (1-2)

过度拆分=假阴性 (1-2)

Directionality of edges

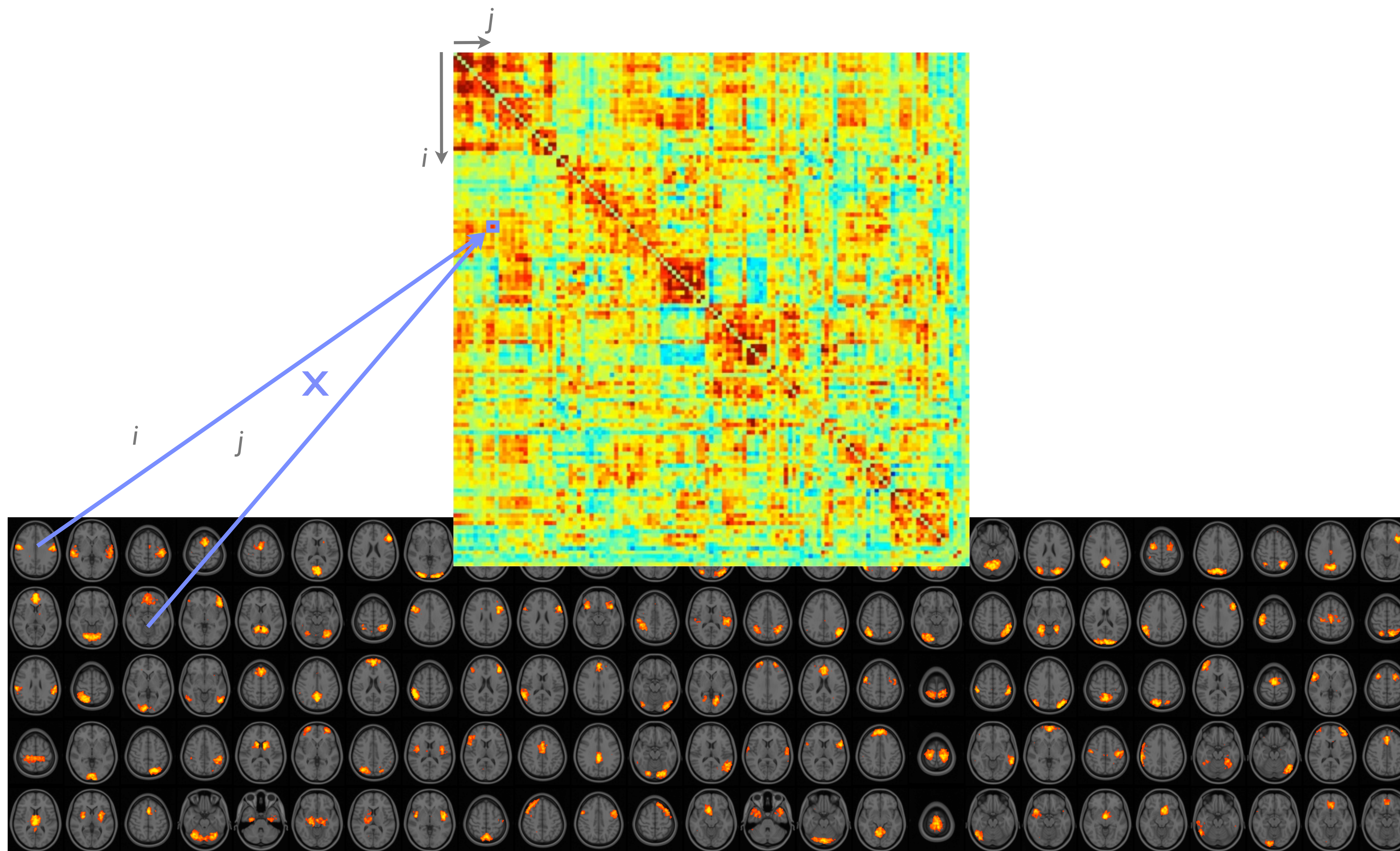
边缘的方向性

- Directionality is hard to estimate in BOLD data 在BOLD数据中难以估计方向性
- Don't use lag-based methods such as Granger causality
不要使用基于事后方法，例如格兰杰因果关系
- Perhaps directionality is oversimplistic view of neural connectivity (particularly in resting-state)?
也许方向性是神经连接过于简单的观点（特别是在静止状态下）？



Building a network matrix

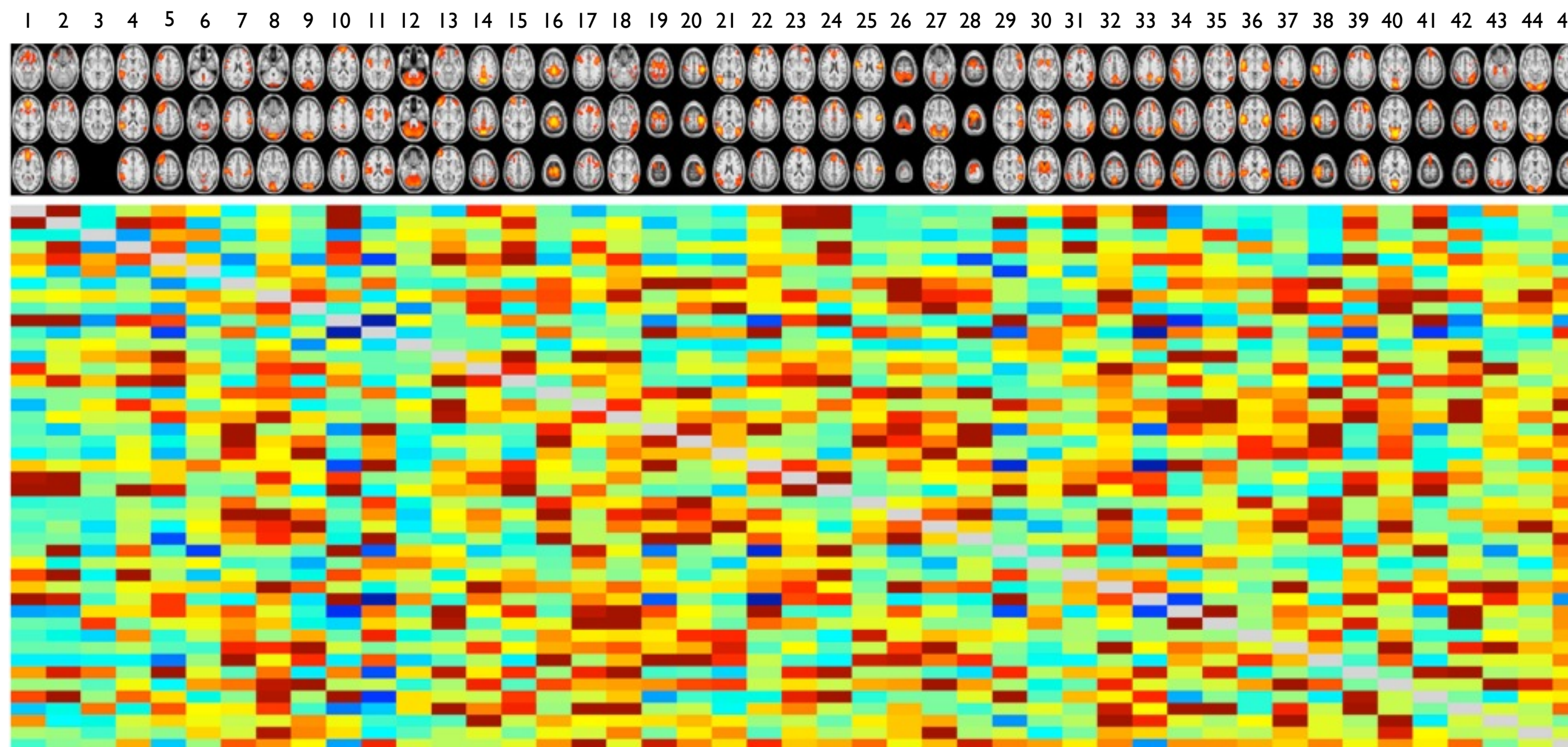
构建网络矩阵





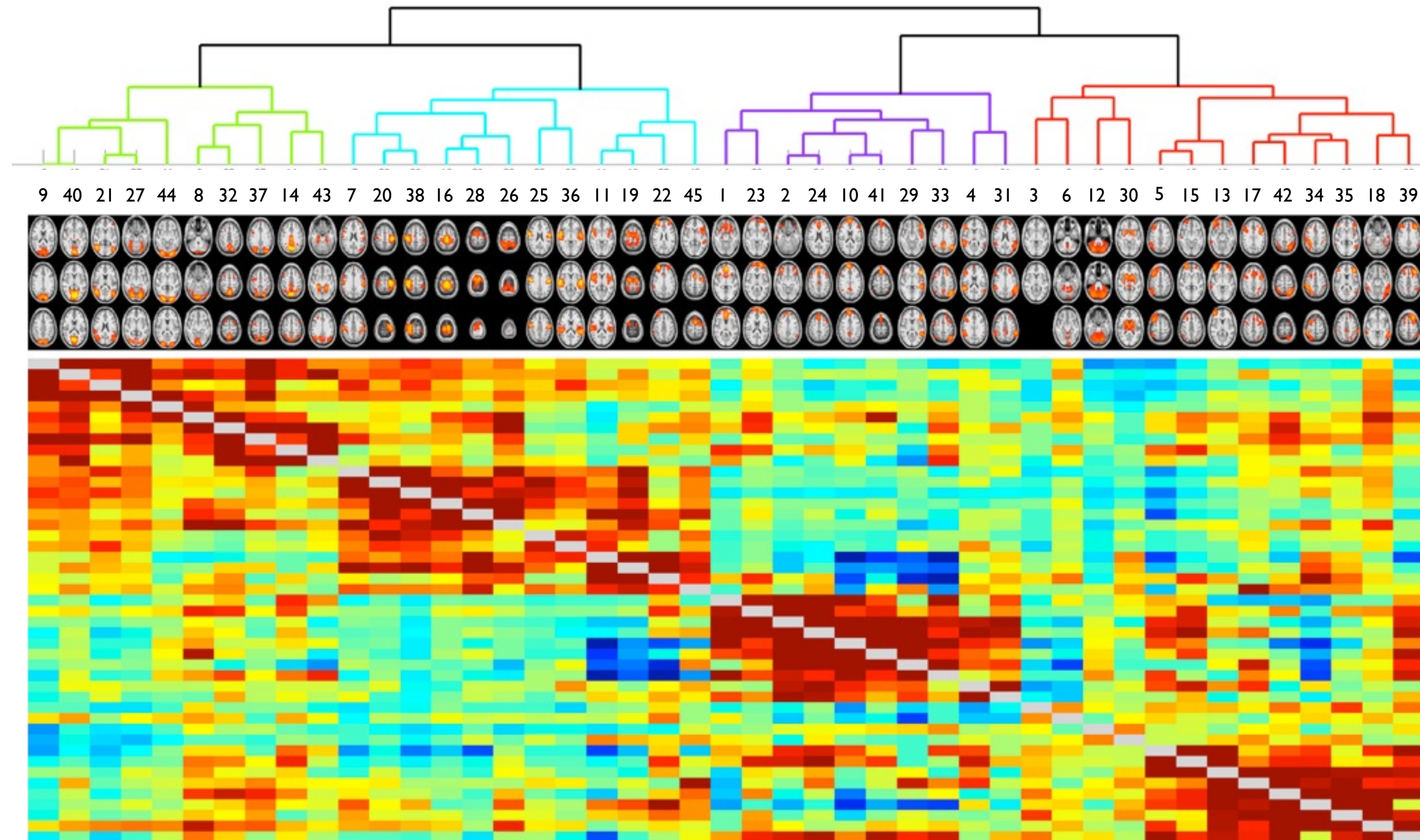
Network matrix

网络矩阵



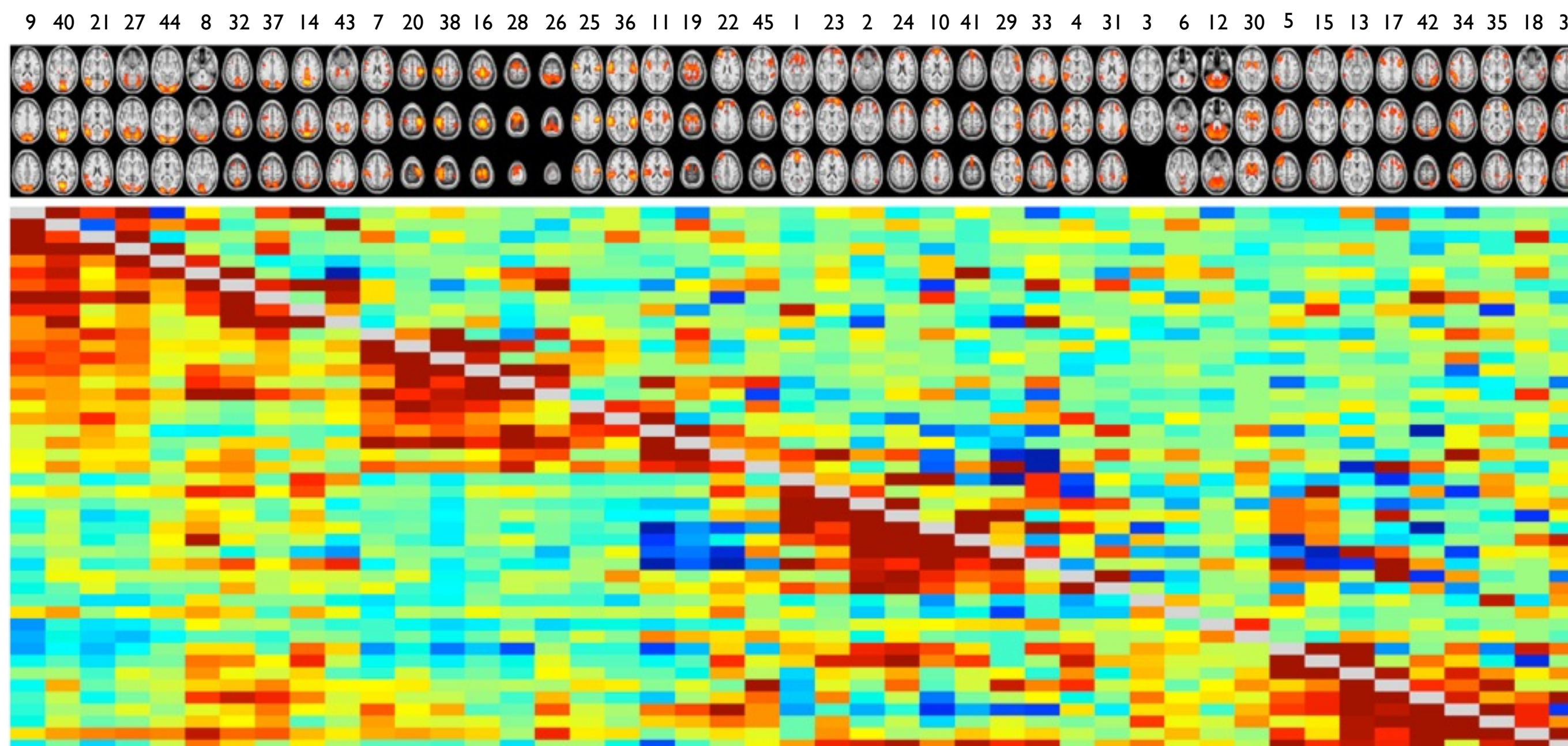
Hierarchical clustering

分层聚类



Partial correlation is sparser than full

部分相关比完全相关更少见



Full correlation matrix

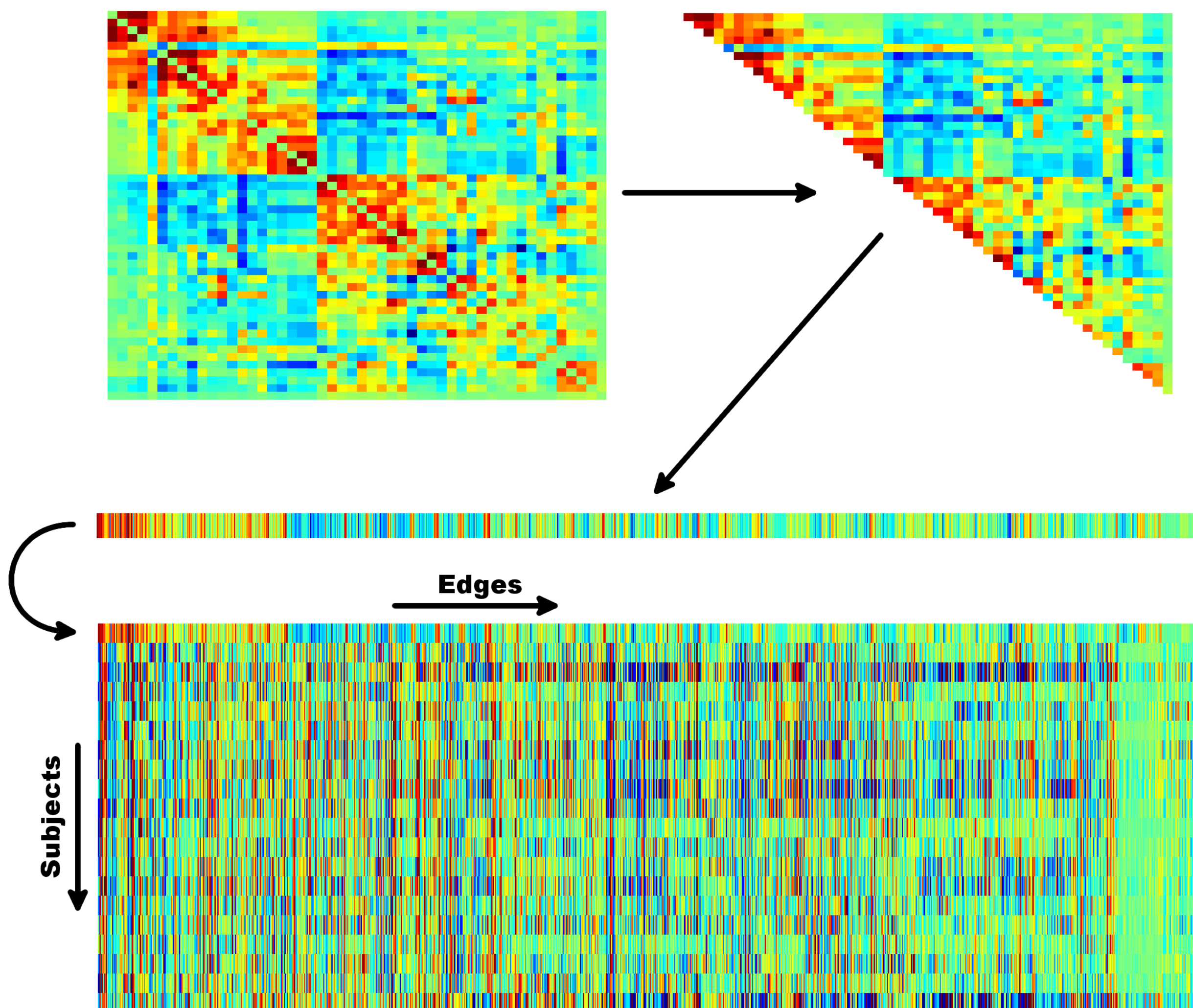
完全相关矩阵

Partial correlation matrix

偏相关矩阵

Group analysis

组分析



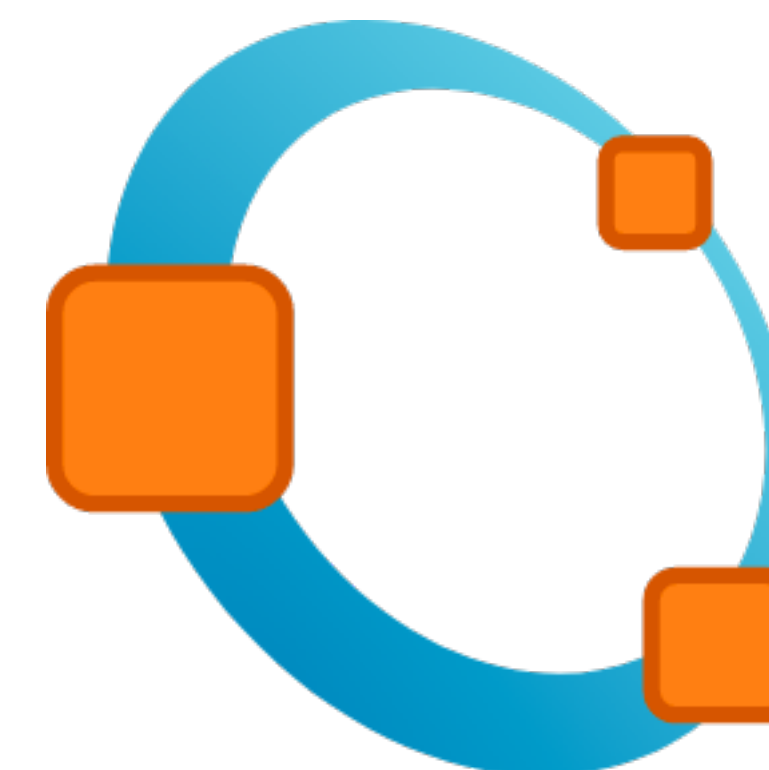
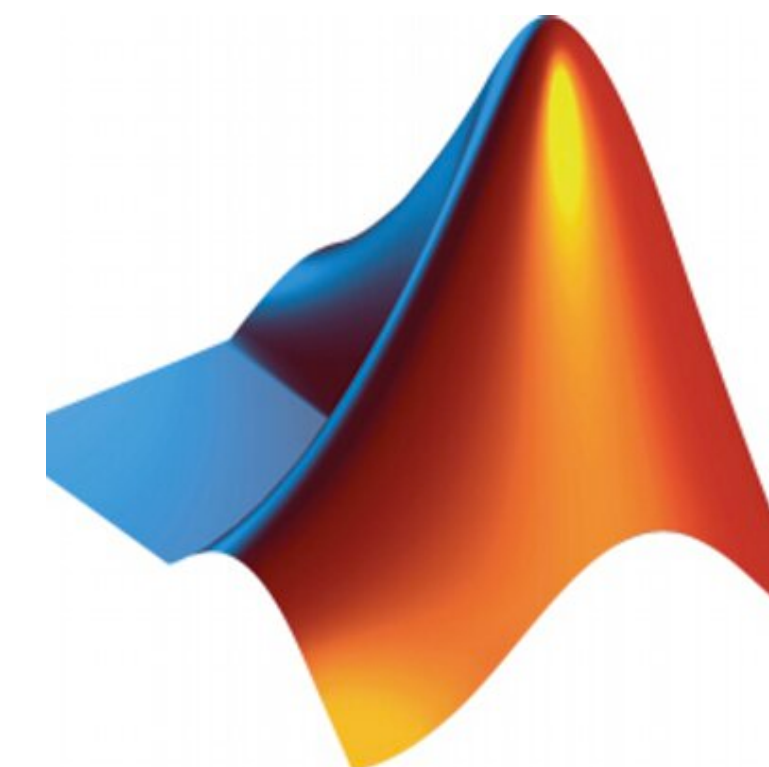
- Calculate network matrix for each subject 计算每个被试的网络矩阵
- Combine all network matrices into one 将所有网络矩阵合并为一个
- Perform group-level comparisons: 组分析
 - Univariate tests for each edge (GLM) 每条边的单变量测试 (GLM)
 - Multivariate prediction methods (SVM) 多变量预测方法 (SVM)



FSLnets

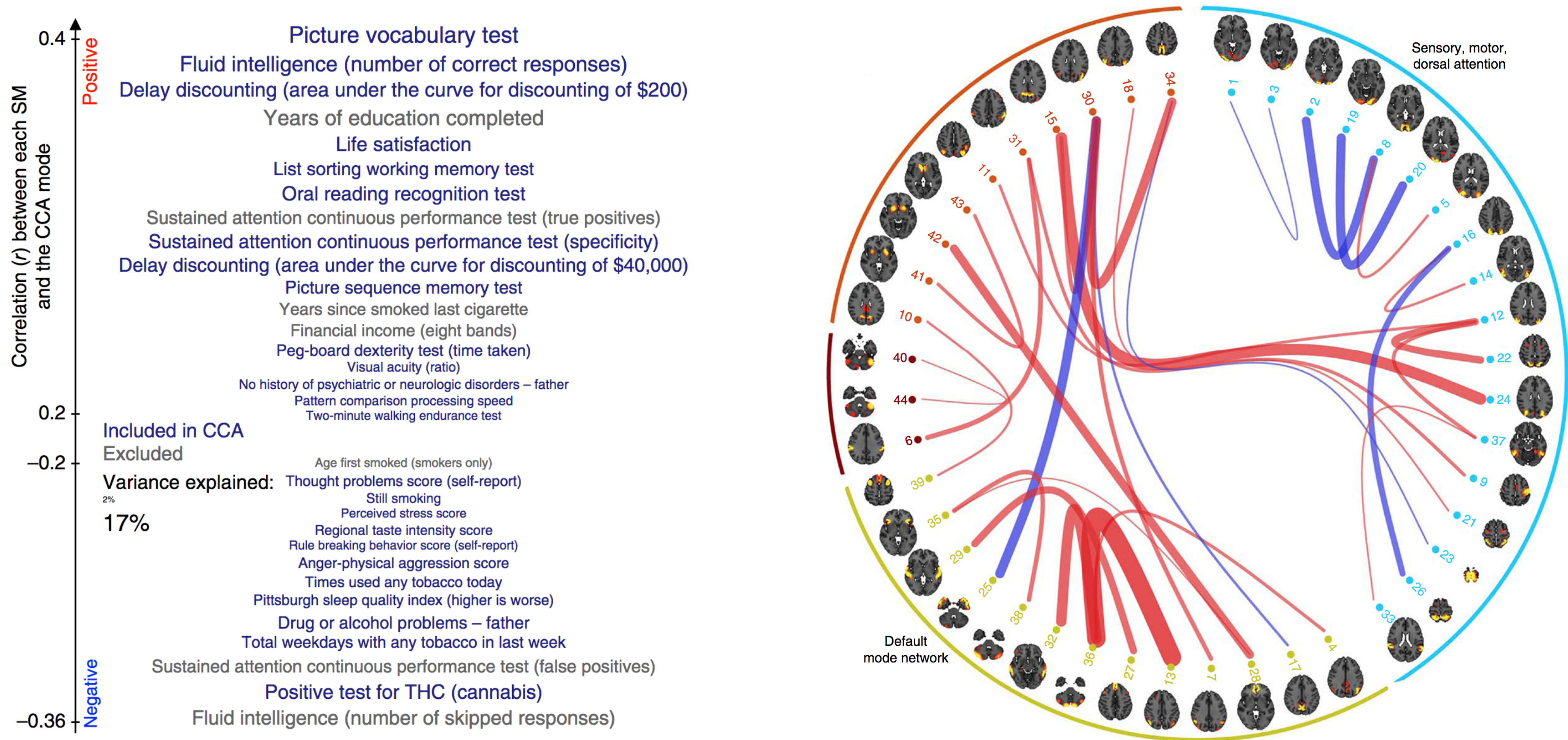
fsl网络分析

- Currently uses Matlab or Octave 目前使用Matlab或Octave
- Therefore this practical will be a bit different from other practicals 因此，这种分析方法与其他方法略有不同
- More information and download here: 更多信息及下载地址: <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets>



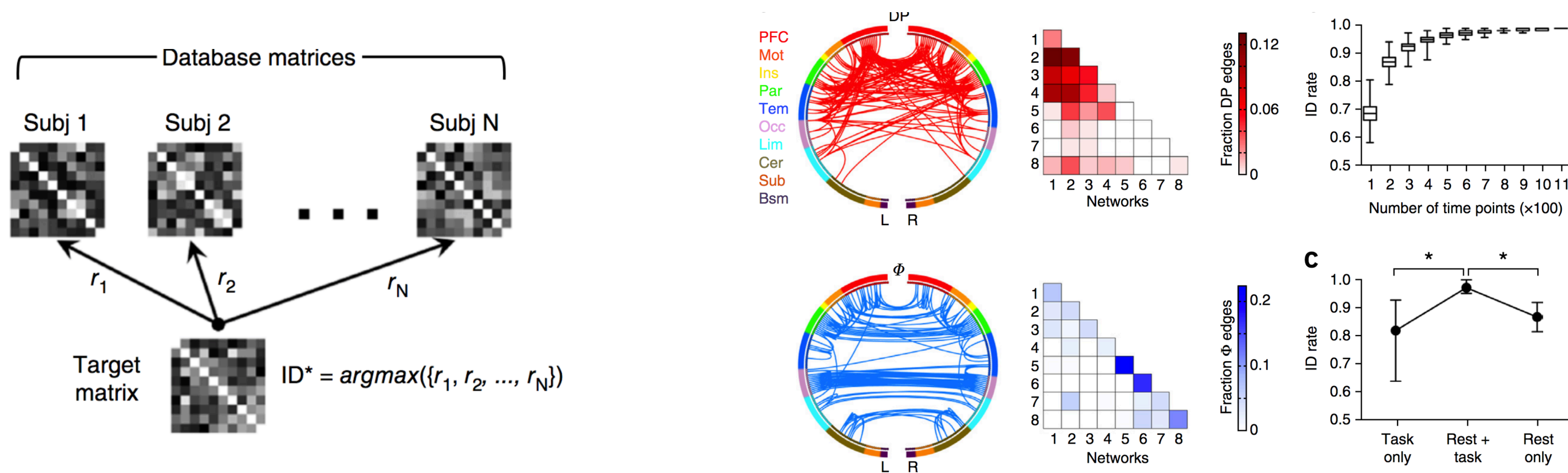
Example: positive-negative mode

例如：正负模式



Example: connectivity fingerprint

示例：脑连接的指纹图谱



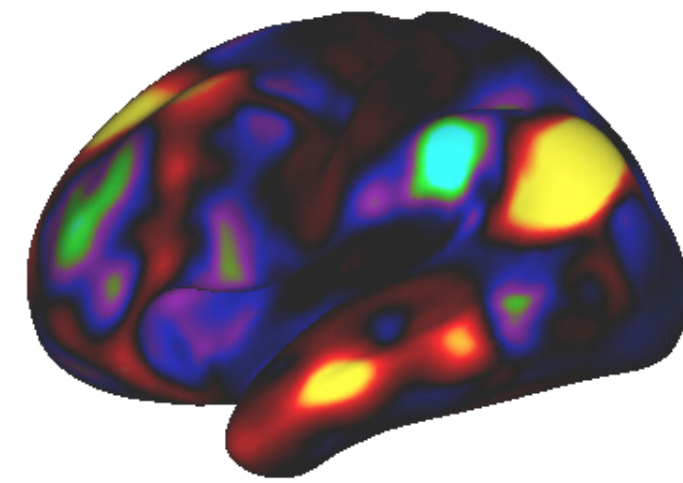


Comparison of methods

方法比较

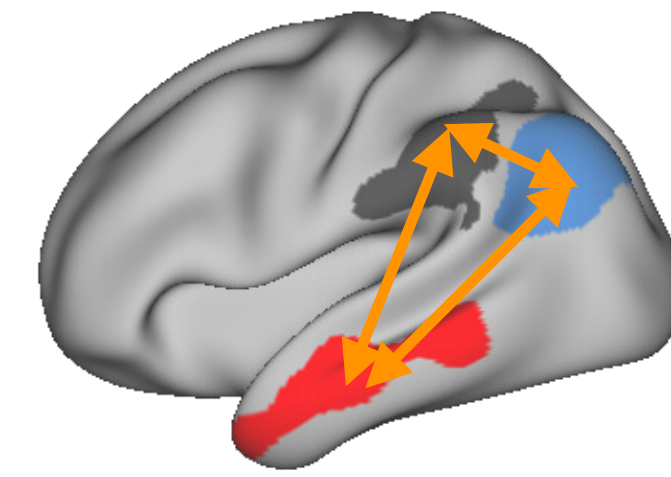
Overview of resting state methods

静息态方法的概况



Voxel-based 基于体素

- Seed-based correlation analysis 基于种子点的相关分析
- Independent component analysis 独立成分分析
- Amplitude of low frequency fluctuations 低频波动的幅度
- Regional homogeneity 局部一致性



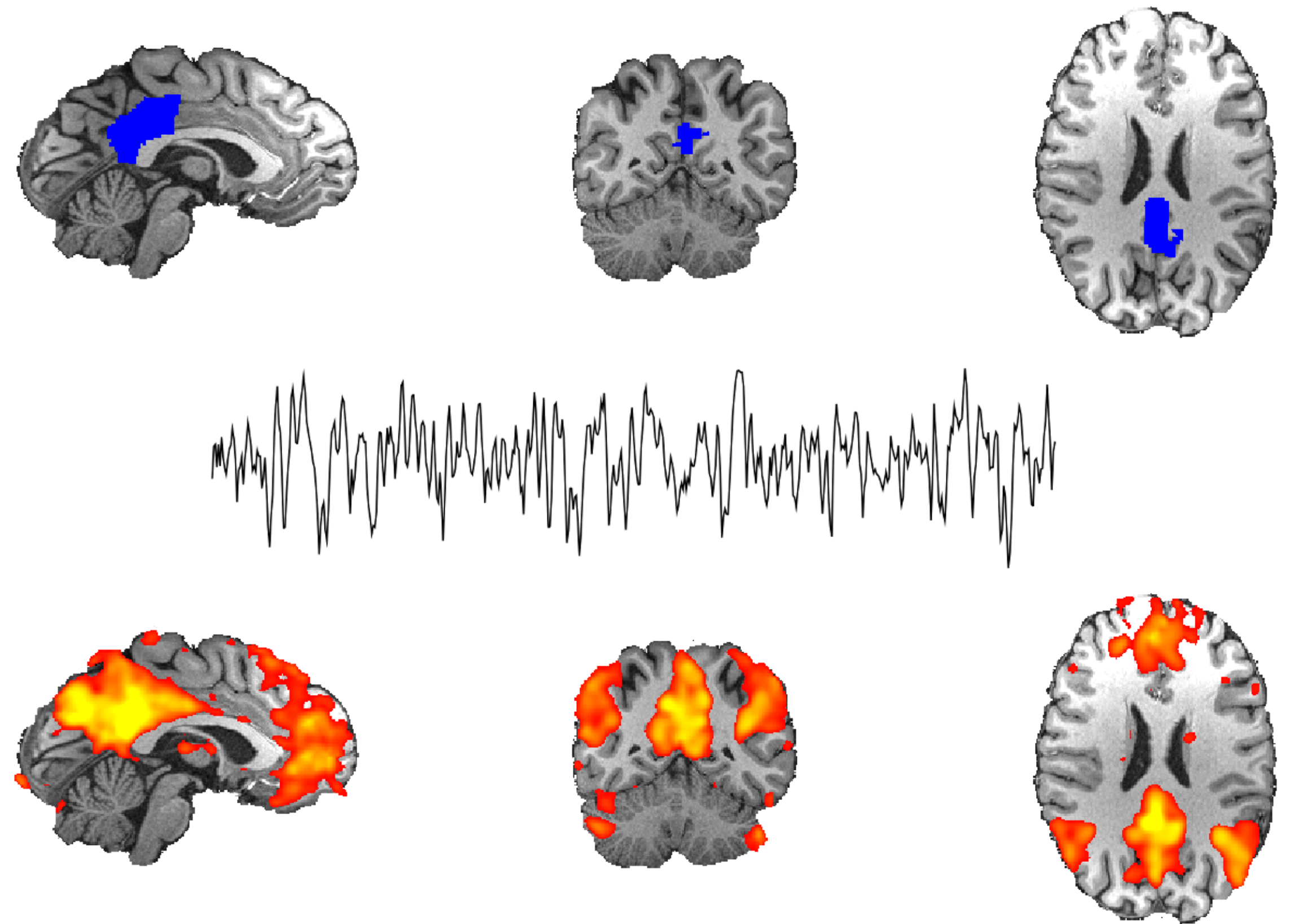
Node-based 基于节点

- Network modelling analysis 网络建模分析
- Graph theory analysis 图论分析
- Dynamic causal modelling 动态因果建模
- Non-stationary methods 非稳定的方法

Seed-based correlation

基于种子点的相关分析

- Easy to interpret 易于解释
- No correspondence problem 没有一致性问题
- Seed-selection bias 种子点选择偏差
- Only models seed-effect (ignoring complex structure & noise) 只模拟种子点效应 (忽略复杂的结构和噪音)

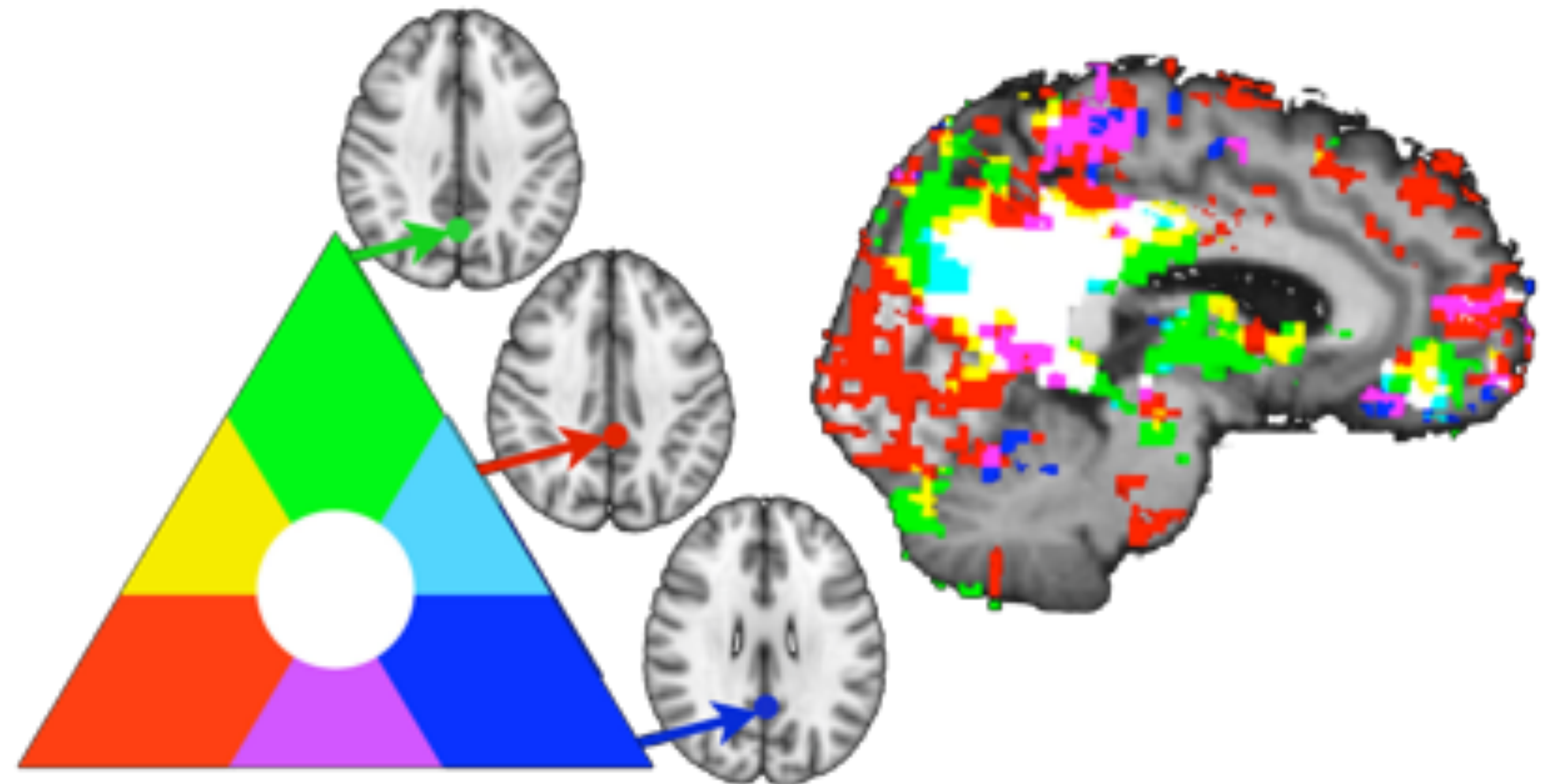


Seed-selection bias

种子点选择偏差

Seed-based correlation results are strongly influenced by small changes in seed location

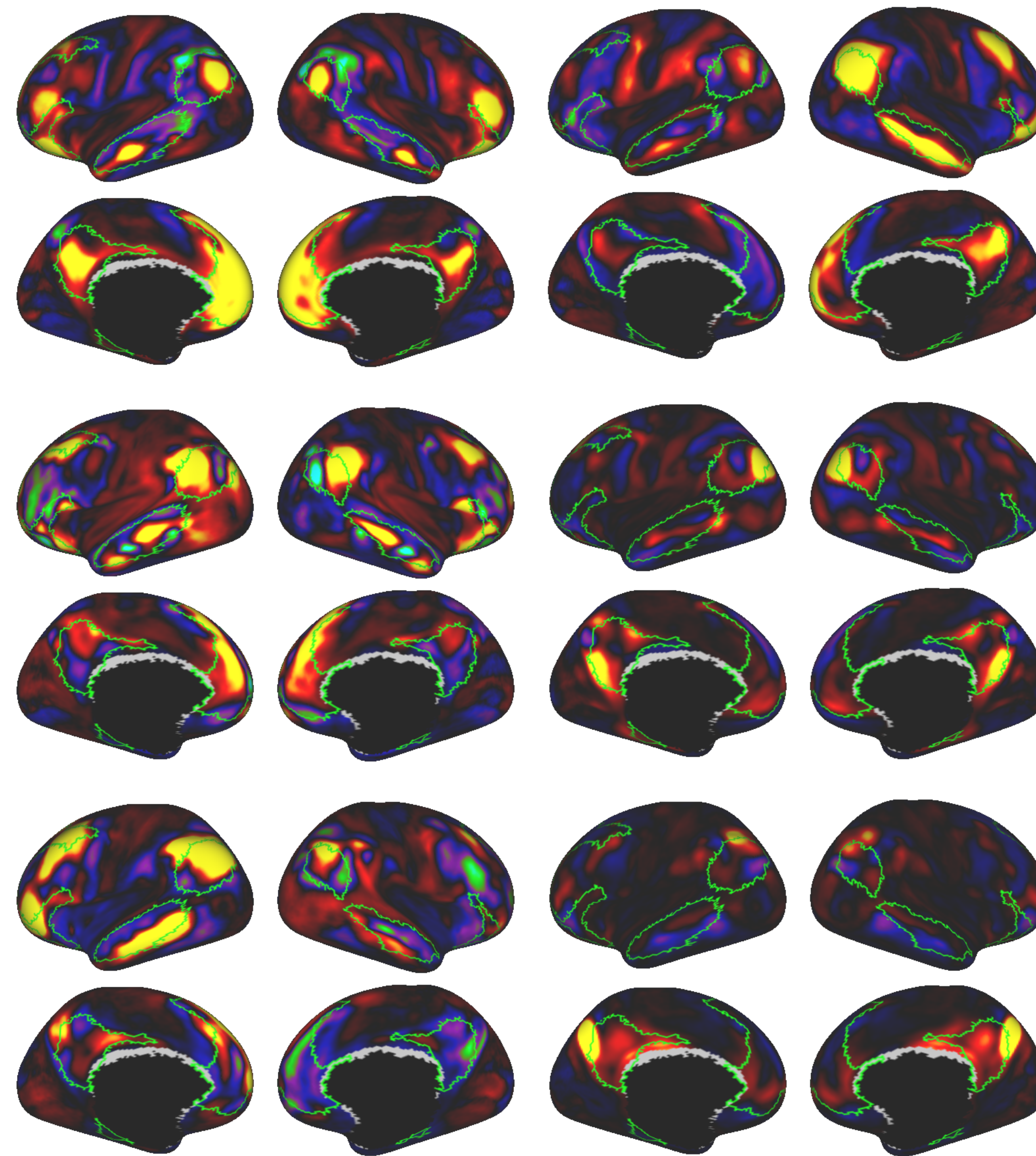
基于种子的相关结果受种子位置的微小变化的强烈影响



ICA

独立成分分析

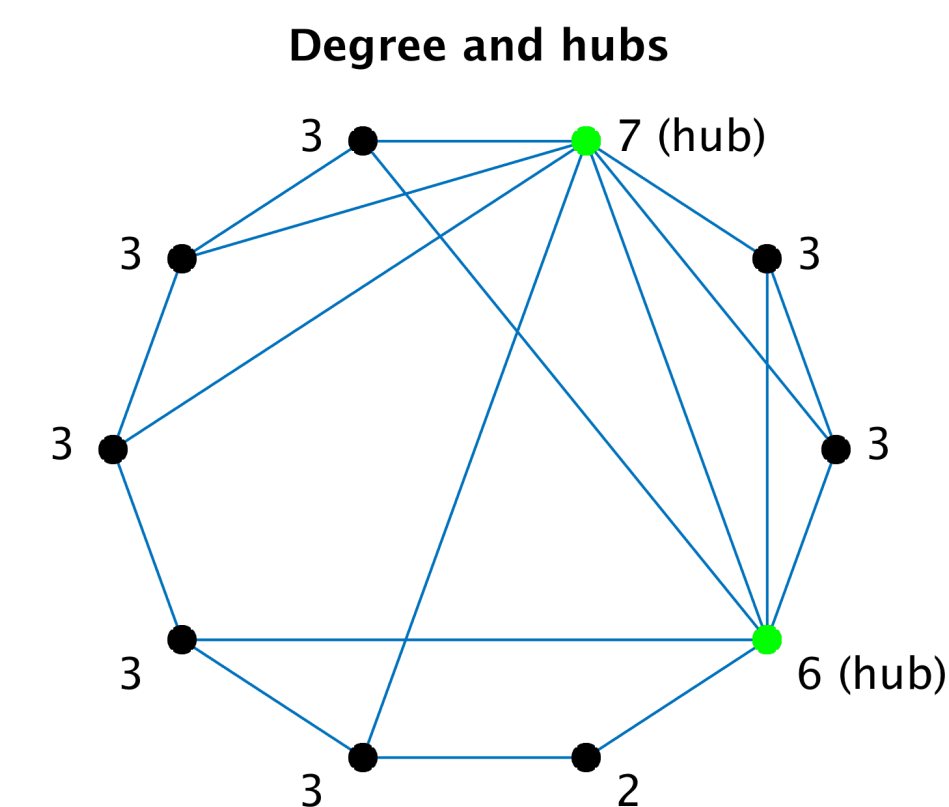
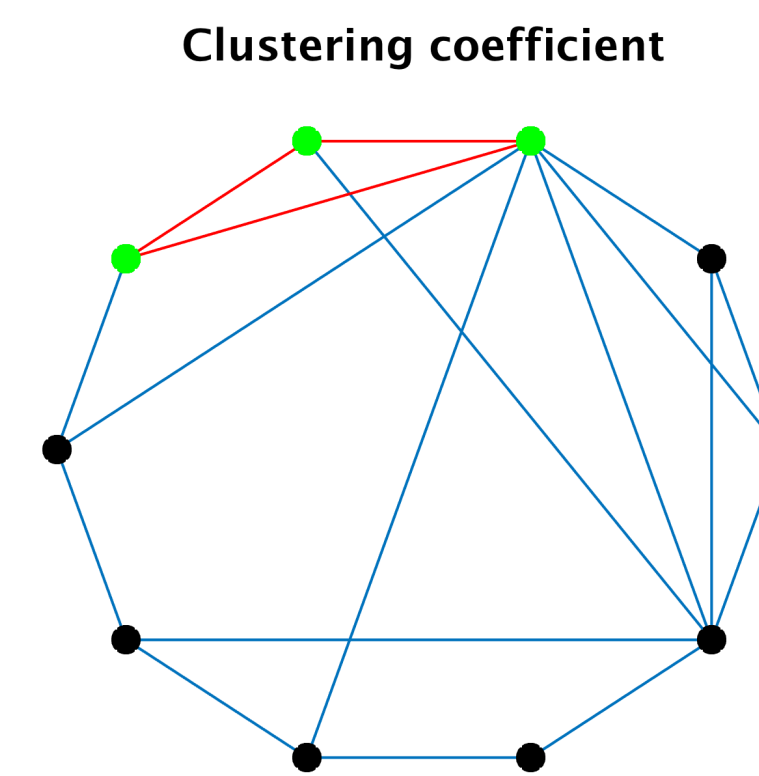
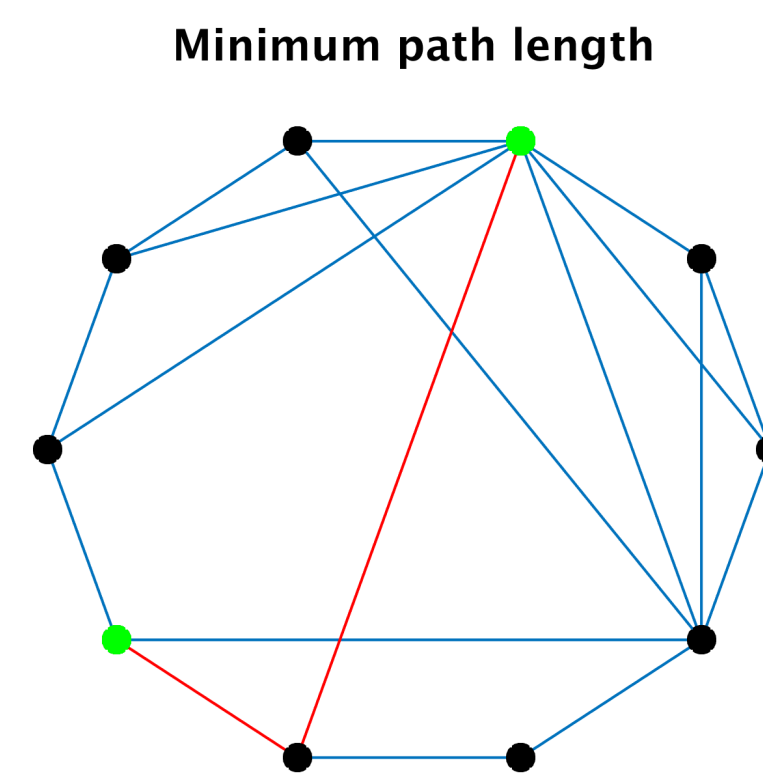
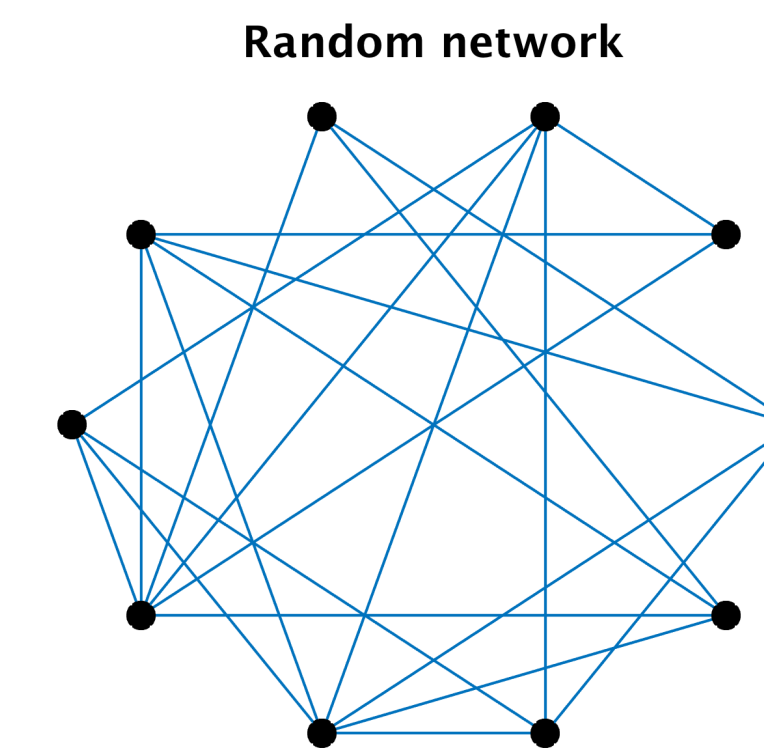
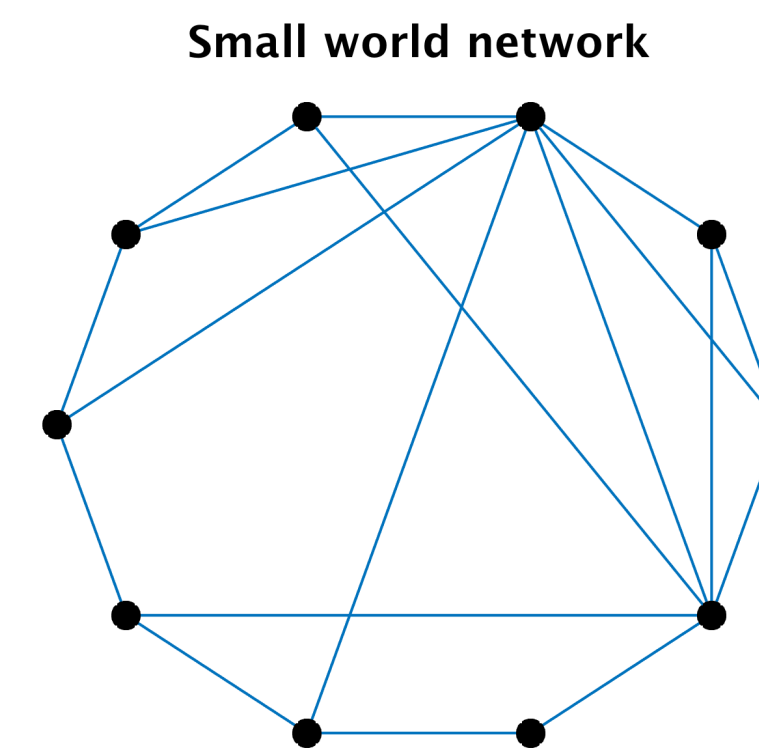
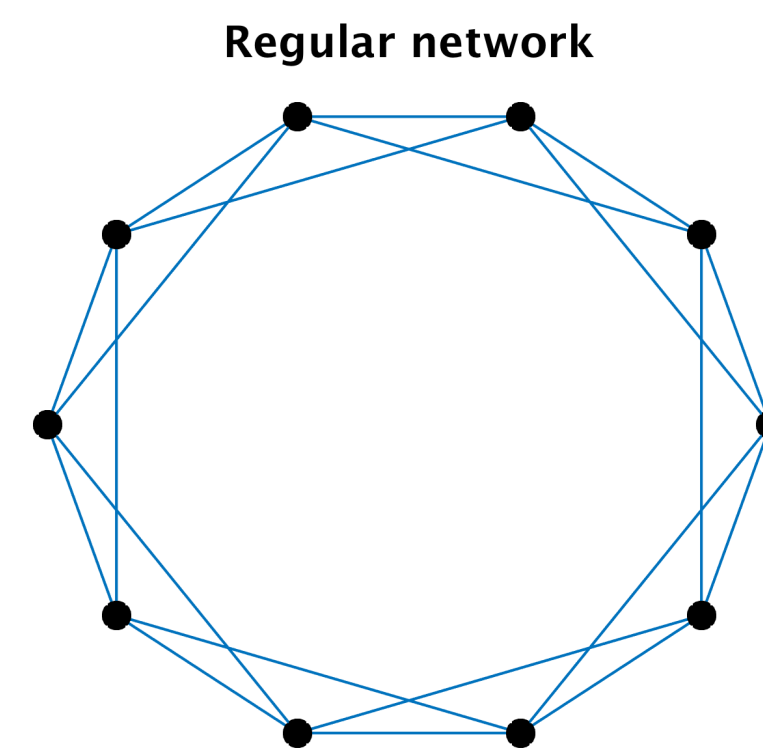
- Multivariate: decompose full dataset
多变量：完全分解数据集
- Test for shape & amplitude
测试形状和振幅
- Can be hard to interpret 可能难于解释
- No control over decomposition (may not get breakdown you want)
成分无法分解（可能无法获得您想要的）



Graph theory

图论

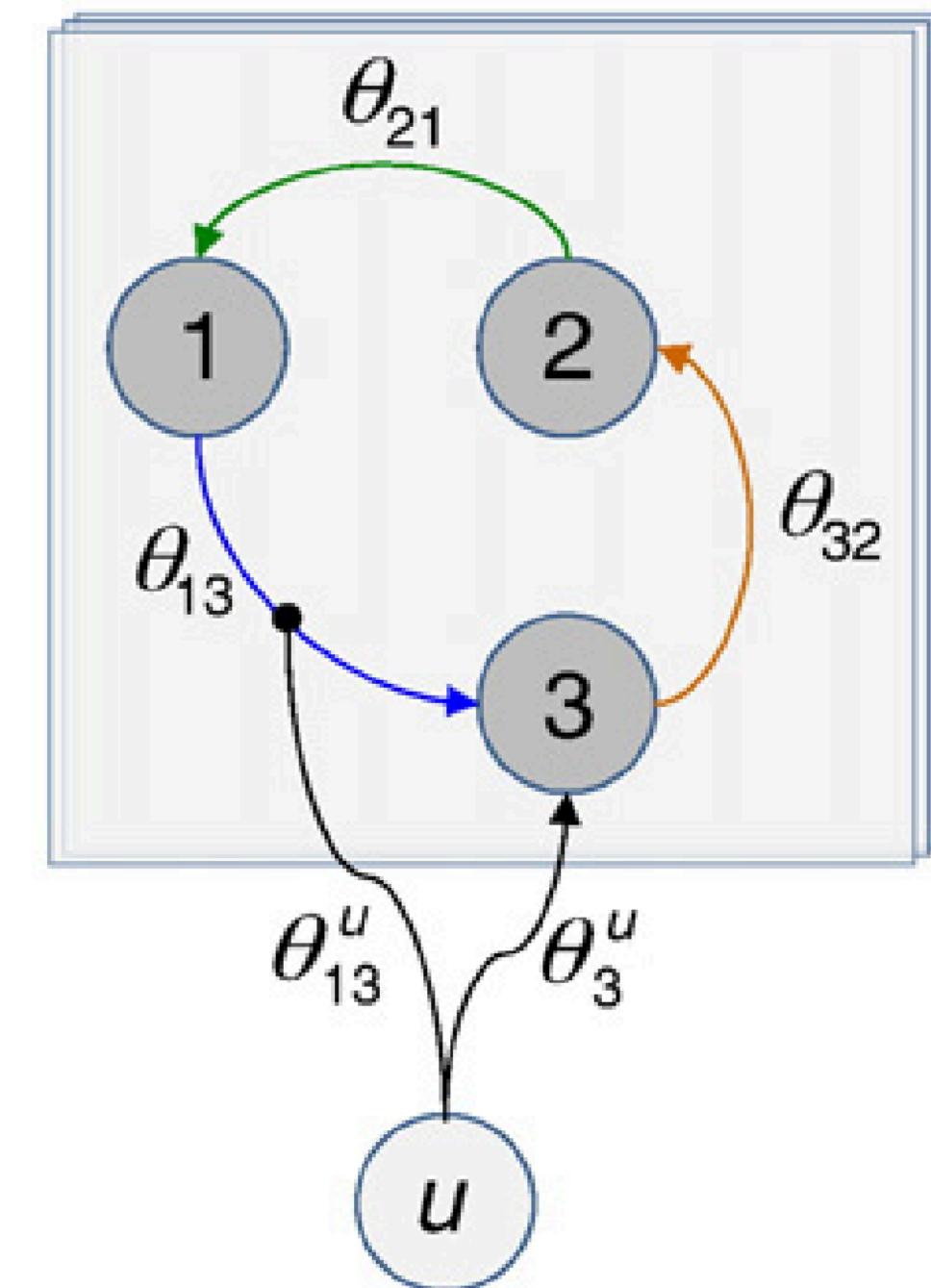
- **Simple summary measures (derived from network matrix) 简单的汇总方法 (源自网络矩阵)**
- **Network matrix often binarised 网络矩阵经常被二进制化**
- **Difficult to meaningfully interpret (abstract and far removed from data) 很难有意义地解释 (抽象和远离数据)**



Dynamic causal modelling

动态因果模型

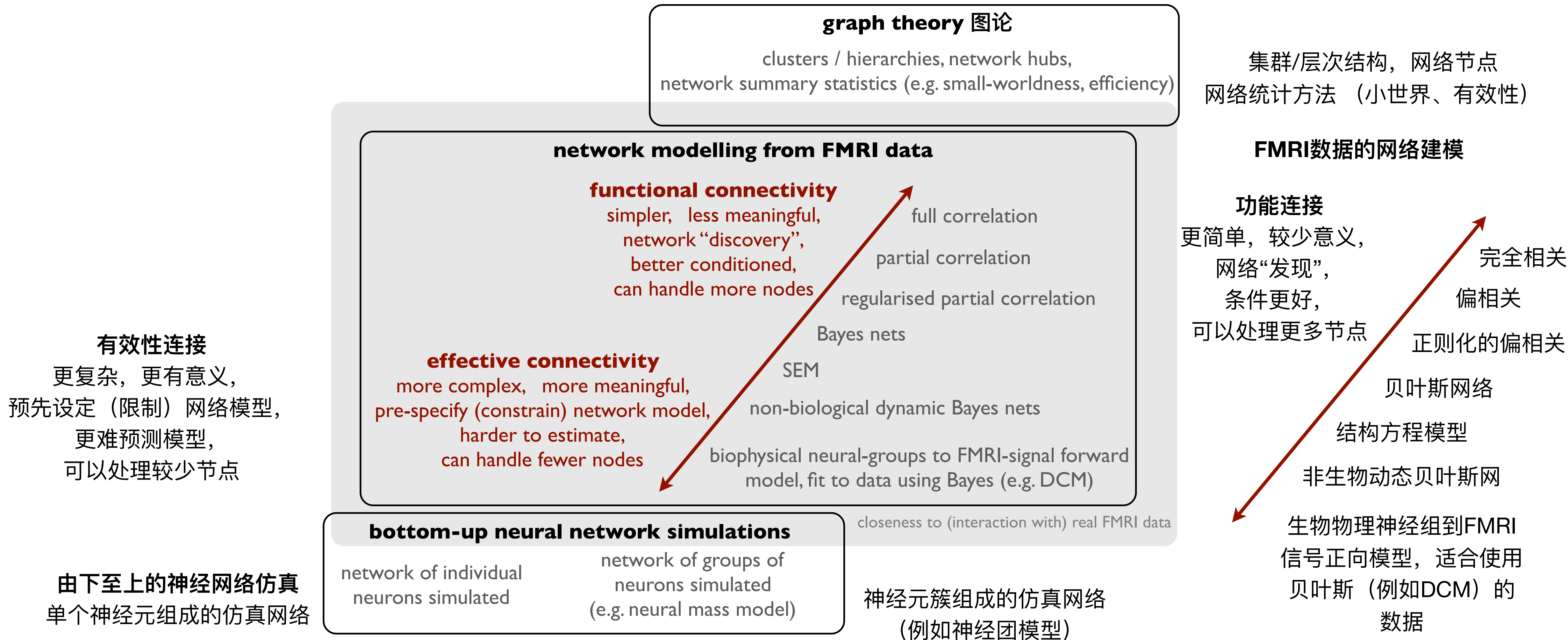
- Directional interpretation (effective connectivity)
定向解释 (有效连接)
- Biophysical model 生物物理模型
- Assumes HRF homogeneity 假设HRF同质性
- Limited model comparisons 有限的模型比较





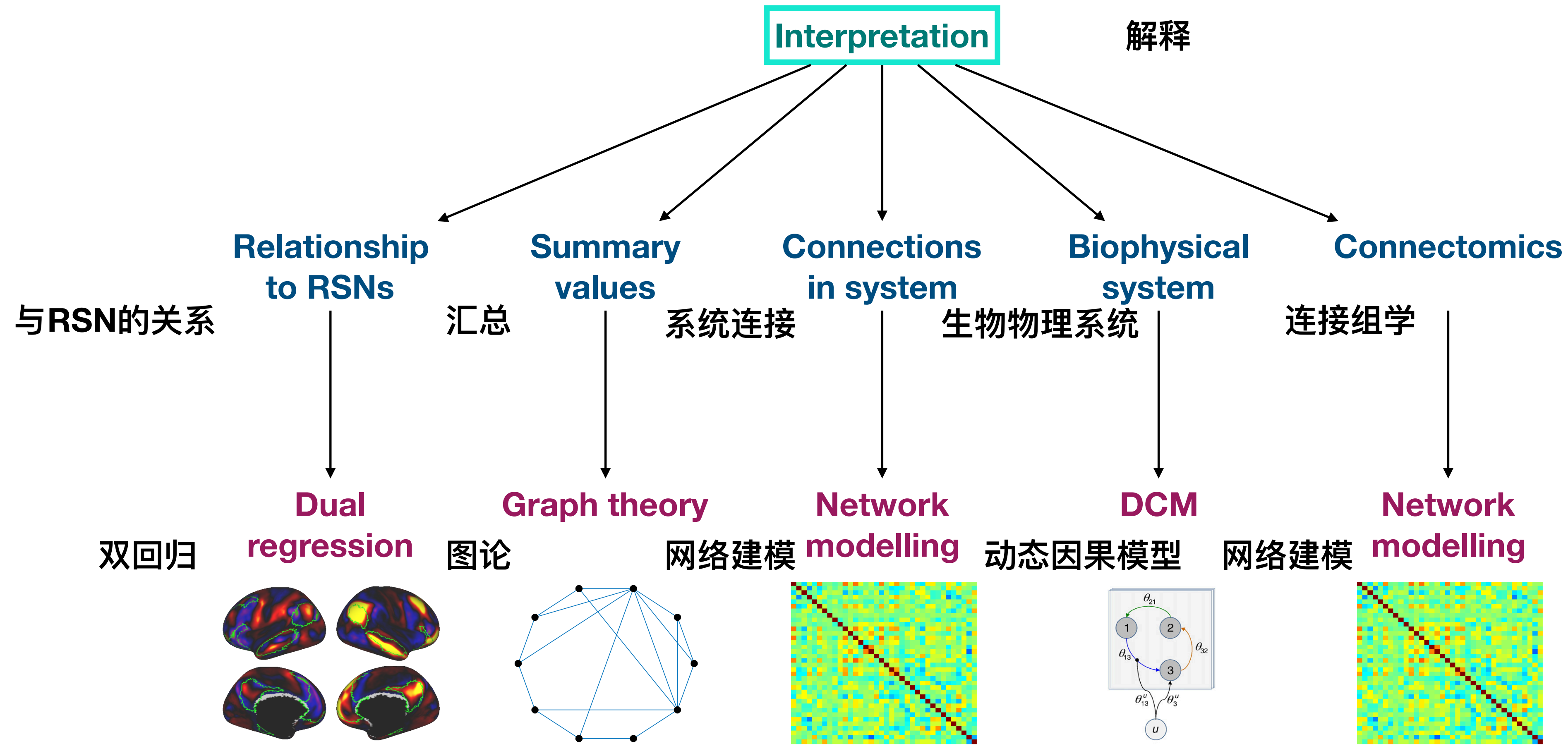
Overview of node-based methods

基于节点的方法概述



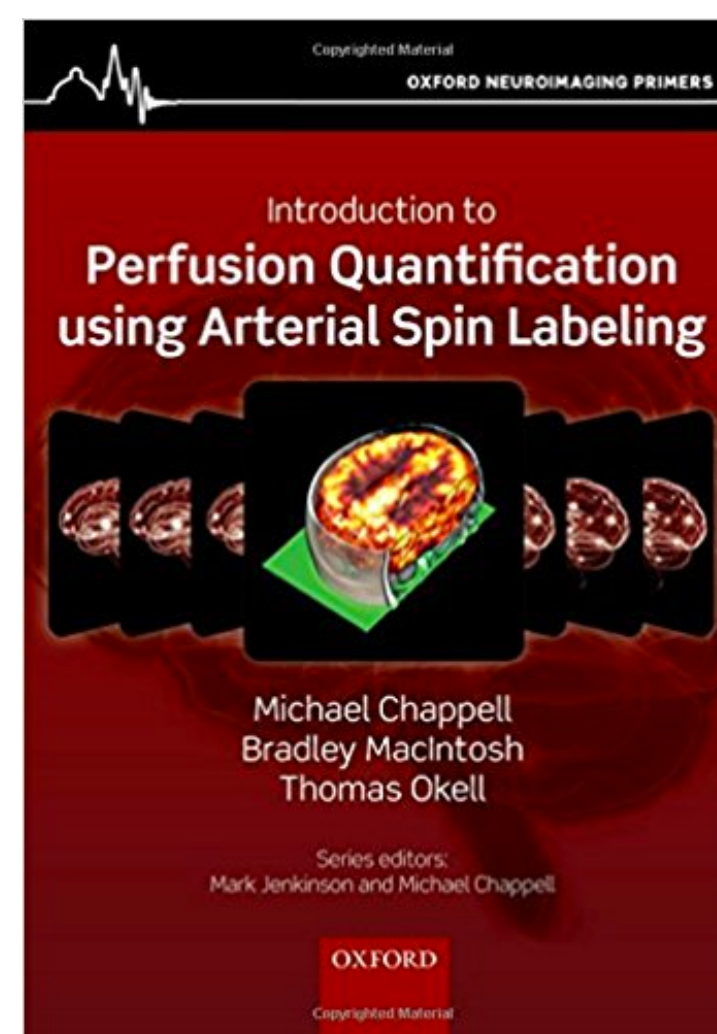
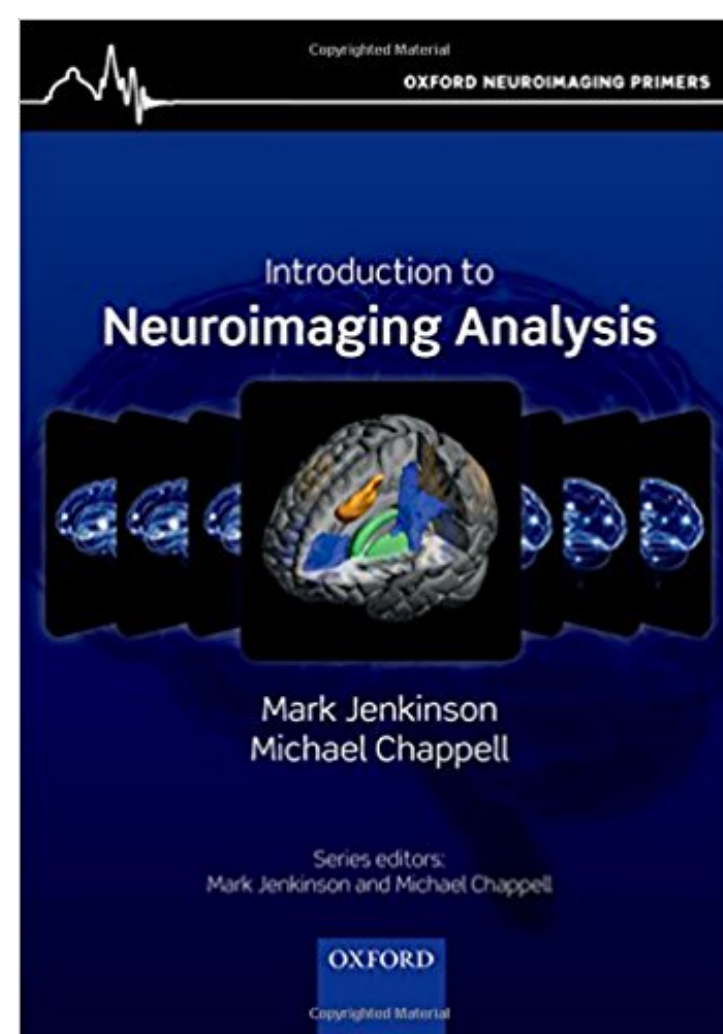
Which method to chose?

选择哪种方法?



The book

- Part of a series of Oxford Neuroimaging Primers — 一系列牛津神经影像引物的一部分
- Available from Amazon and Oxford University Press 可从亚马逊和牛津大学出版社获得
- Free material available on primer website: <http://www.neuroimagingprimers.org/>
- Please consider writing a book review on Amazon



That's all folks

